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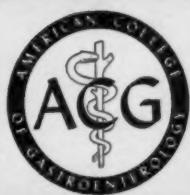
Ulcerative Colitis in the Aged

Carcinoma of the Colon

Palliation in the Management of Carcinoma
of the Colon and Rectum

Studies of Systemic Hemostatic Factors
in Patients with Bleeding Duodenal Ulcer

Twenty-sixth Annual Convention
Cleveland, Ohio
22, 23, 24, 25 October 1961



Official Publication
AMERICAN COLLEGE
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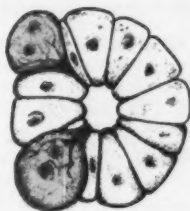
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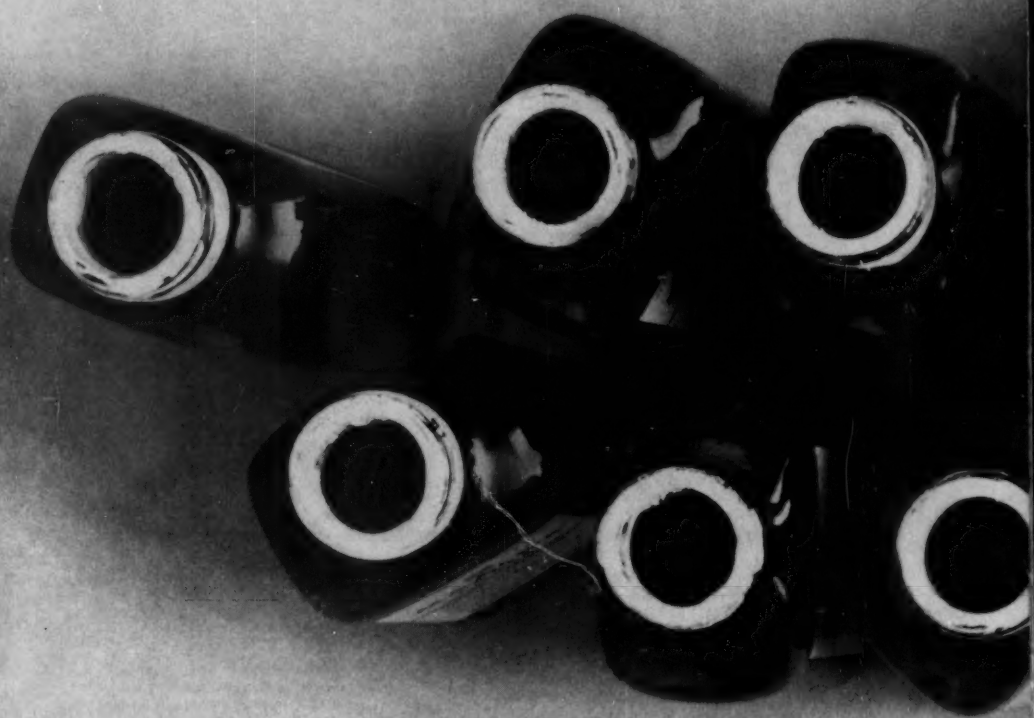
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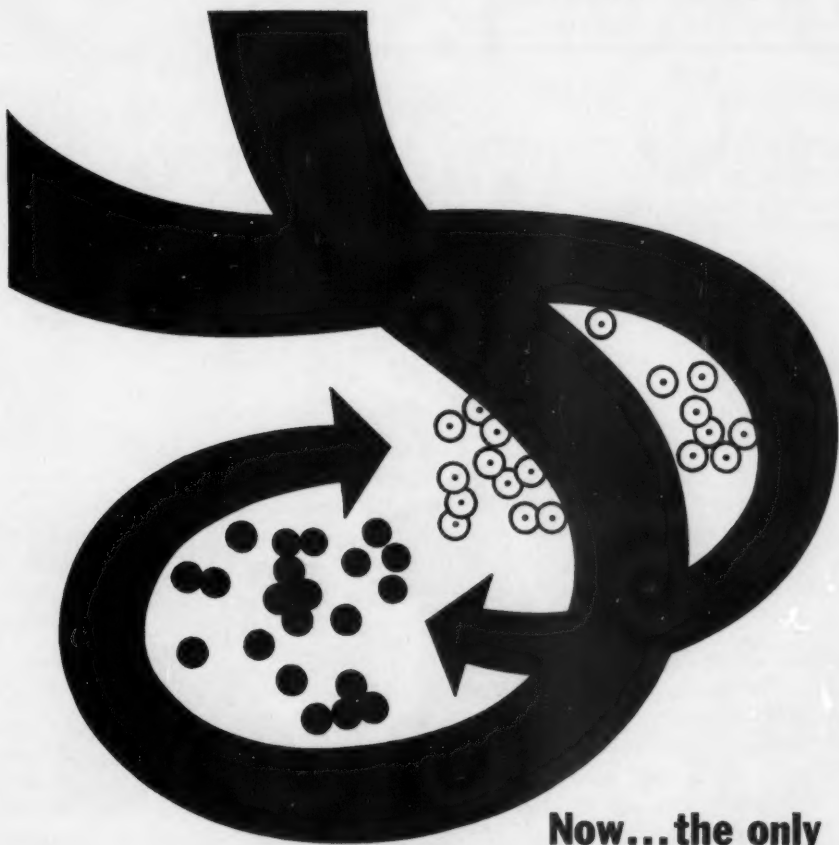
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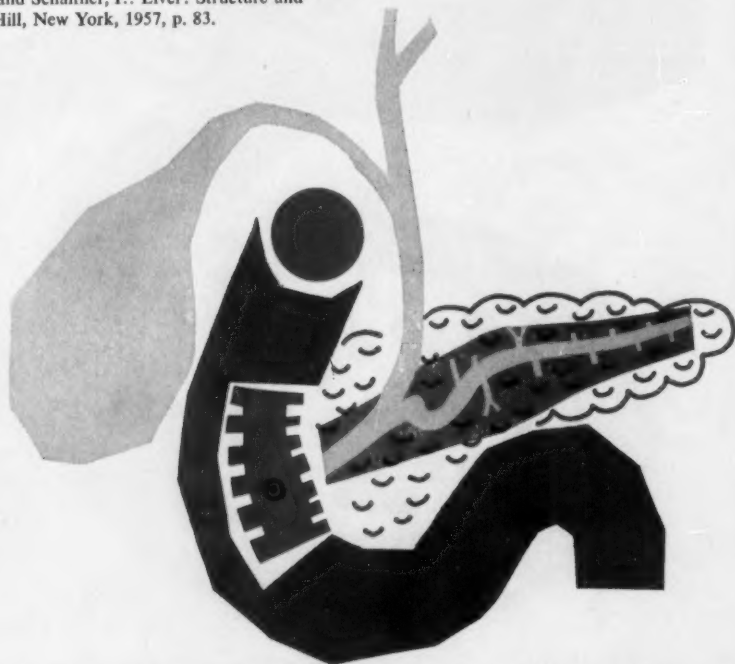
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ULCERATIVE COLITIS IN THE AGED*†

Z. T. BERCOVITZ, M.D.

La Jolla, Calif.

Ulcerative colitis may occur in the aged without premonitory symptoms as an acutely fulminating form of the disease with blood, mucus, pus, fever, hemorrhage and distention of the abdomen. It may be so rapidly progressive as to become a surgical emergency within the first year or cause the death of the patient.

The mode of onset is variable. In the aged it is not uncommon to see individuals with evidences of colon obstruction at the level of the sigmoid. Others may have an acute toxic megacolon and all the signs and symptoms of the fulminating form of the disease. Some have clinical evidences of impending perforation or may even perforate within a relatively short time of the onset. Massive hemorrhage as the first sign of ulcerative colitis has been a frequent occurrence. Watery diarrhea which quickly dehydrates the patient and causes a medical emergency is one of the most frequent modes of onset. In many of these patients the early x-ray signs are minimal but subsequent studies confirm the diagnosis of ulcerative colitis.

The location of the first evidences of the disease may be in the rectum and sigmoid or even involve a small segment of adjoining distal descending colon. There may even be partial obstruction due to inflammatory spasm at the junction of the sigmoid and descending colon. In most of these patients the disease is quite mild if well controlled. There does not appear to be a positive relationship between acute diverticulitis of the sigmoid and true ulcerative colitis of this area.

Older age patients may have suffered with chronic ulcerative colitis for many years. In a recent study¹ it was found that patients had the disease for

*Read before the 25th Annual Convention of the American College of Gastroenterology, Philadelphia, Pa., 24, 25, 26 October 1960.

†Dr. Bercovitz moved to California before the Convention and so was not present in person. The paper was read for him by Dr. Sidney M. Rogers, Chief Medical Resident at the Albert Einstein Medical Center.

periods of 10 to more than 30 years. These patients had frequent relapses and remissions but as they approached the older periods of life the most striking changes appeared in the x-ray films. These will be reported in detail³ but briefly, during the earlier years ulcerations were demonstrated roentgenologically and there were changes in the mucosal patterns typical of acute and chronic inflammation. Later on the x-ray films showed evidences of stricture, narrowing, alternating areas of dilatation and spasm but no mucosal patterns could be demonstrated and no definite ulcerations were seen. In some of those who came to autopsy there was complete loss of mucosa and the colon lining was replaced with squamous epithelium. In some of the older patients the replaced mucosa was in longitudinal ridges lying in the long axis of the bowel. In many of these patients the typical ulcerative colitis symptoms were replaced by episodes of partial obstruction alternating with diarrhea. In other patients there was chronic constipation with some distention due to the narrow areas especially in the descending colon. Many of these patients died from conditions unrelated to the ulcerative colitis.

DIFFERENTIAL DIAGNOSIS

Malignancy of the colon is one of the most important conditions to be considered in the differential diagnosis. This diagnosis is not always easily accomplished. Repeated sigmoidoscopic examinations and x-ray studies with air double contrast must be made. Carcinoma may occur in any portion of the colon and may not necessarily be related to the ulcerative colitis.

Diverticulosis and diverticulitis are much more frequently observed in the aged. Acute and chronic forms of ulcerative colitis may occur independently of these conditions or may complicate them. It has been a fairly frequent experience in reviewing a series of x-ray films³ of ulcerative colitis where serial studies have been made over a period of years to observe the disappearance of the diverticula as the chronic forms of ulcerative colitis have developed. When scar tissue, shortening and narrowing develop in the colon, the diverticula disappear.

Terminal ileitis may be associated with ulcerative colitis. In some cases, segmental colitis of the right side has been present, while in others the entire colon has been involved. In some cases the microscopic pathology of both the right colon and the terminal ileum has been quite similar.

Bleeding from the bowel is most commonly due to *carcinoma, diverticulitis, polyposis, chronic ulcerative colitis, duodenal or gastric ulcer, gastric carcinoma, or esophageal varices*. Among the less common cases is *hemangiomata* either localized or generalized throughout the small or large intestine. This condition also known as the Weber-Osler-Rundel syndrome, may occur more often than previously suspected, especially in females well beyond the menopause where it is apparently related to failure of estrogenic hormones. *Small bowel polyposis,*

(Peutz-Jeghers syndrome), *telangiectasis* of the small or large intestine and *mesenteric thrombosis* are other causes of bleeding.

Carcinoma anywhere in the gastrointestinal tract may either simulate ulcerative colitis or complicate it. Rectal and sigmoid neoplasms are those which most commonly cause symptoms suggestive of ulcerative colitis.

Carcinoid tumors of the gastrointestinal tract are usually located in the region of the appendix and cecum. In addition to diarrhea, cutaneous flushing may appear anywhere on the body and last for varying periods of time. The flushing may be related to hot drinks, alcohol, eating or bowel movements, and may also at times be precipitated by palpation of the enlarged liver. Diarrhea may vary from a few movements to 20 or 30 times in 24 hours. Blood has not been reported in these cases. The diagnosis is made by finding 5-hydroxy-3 indole-acetic acid (Serotonin) in the urine.

Staphylococcus enterocolitis following the administration of various antibiotics may develop and resembles acute ulcerative colitis. *Shigella* (bacillary) dysentery and amebic dysentery also have to be considered. Duodenal ulcer, gastric ulcer or carcinoma of the stomach are frequently associated with diarrhea, especially in older age patients. Chronic pancreopathy and malabsorption syndromes also are included in the differential diagnosis.

COMPLICATIONS

The most serious problems with this entire group of patients lie in the secondary or complicating conditions usually related to the ageing process. Diabetes is one of the most serious of these conditions. The use of steroids in therapy has to be most guarded in the face of diabetes. Arteriosclerotic heart disease, hypertension, arteriosclerosis, cardiovascular renal complications and chronic liver disease are all problems which add to the seriousness of the ulcerative colitis and also hamper therapeutic efforts.

PROGNOSIS

In the aged, the prognosis of ulcerative colitis is directly related to the age at onset of the disease¹. All of the patients whose first symptoms were in the 70's died within the first year of the disease. Of those whose onset was between 60 and 69 more than one-half went to surgery and of these more than one-half died postoperatively. In the group whose onset was during the 50's, there were no deaths under medical management and only three of the 18 patients reported in this study¹ required surgery. There was 1 death 3 months postoperatively.

In comparison with those whose onset was in later years of life there were 21 patients reported in the study whose onset was under 50 years of age and 76 per cent are in clinical remission. There were only 2 deaths due to carcinoma. Three patients required surgery and are clinically well.

TREATMENT

The treatment of ulcerative colitis in the aged is dependent upon the severity of the process, the complicating factors present and the stage of the disease.

Emergency treatment is quite frequently the rule and must be given vigorously. The clinical emergencies which commonly occur are severe diarrhea, hemorrhage, megacolon with the acutely fulminating forms of the disease, complete physiological systemic degeneration and collapse related to adrenal cortical failure.

Whole blood transfusions, intravenous fluids, electrolyte and protein replacement are the primary indications. Adrenal cortical support is also required. All of these measures must be carried out vigorously but in consideration of whatever other disease may be present such as diabetes or cardiovascular-renal complications. Blood transfusions are required not only to balance that lost by hemorrhage but to insure adequate kidney function, cerebral and coronary circulation. It may be necessary to give continuous transfusions as long as there is evidence of blood loss and until the blood pressure, hemoglobin and hematocrit are stabilized. In some cases it may be necessary to give direct transfusions of fresh blood (without blood bank anticoagulants). In addition calcium, Vitamin K and ascorbic acid are also indicated in adequate amounts. Intravenous premarin in 20 mg. dosages may be given every 30 minutes to one hour until at least 100 mg. are given in a single treatment if the bleeding has not stopped. This therapy may be given in both female and male patients and repeated on the same day or subsequent days as indicated. Intravenous premarin does not take the place of blood transfusions.

During blood transfusions intravenous dosages of benadryl in amounts of 50 mg. to 100 mg. every four hours are indicated both for the effect in helping to prevent transfusion reactions and also for the sedative effect upon the patient.

Fluid replacement by intravenous infusions must be given in adequate amounts and continued as long as there is severe watery diarrhea. Infusions can be used as the vehicles for giving calcium, electrolytes, vitamins and proteins. Adrenal cortical steroids may be added to the infusions also. Benadryl or Dramamine given intravenously at the start of an infusion will reduce the patient's discomfort.

Antibiotic therapy has an important place in the emergency treatment of ulcerative colitis. Chloramphenicol is the antibiotic of choice in dosages of 1 or 2 gm. daily intravenously or by intramuscular injection. Chloramphenicol has been found to be almost a specific in the staphylococcus enterocolitis as well as the acute megacolon with impending perforation.

The use of adrenal corticosteroids during an acute emergency with ulcerative colitis in the aged must be given consideration but only under the most

serious conditions and with the utmost caution. Steroid therapy should be withheld in the face of acute megacolon with impending perforation. Acute sudden perforations have been observed in the wake of the administration of steroids. Once, however, the decision to operate has been made, the situation requires adrenal cortical steroid support during the surgical procedure and in the immediate postoperative periods. Intravenous hydrocortisone in dosages of 100 mg. may be added to the infusions during the operation and supplemental dosages may be required to maintain the systolic pressure. Care should be observed, however, in patients with arteriosclerosis not to push the pressure up to the point where a cerebral vascular accident could occur under anesthesia or during the operation. When emergency operation is done under hypothermia there is much less element of shock both during the surgical procedure and in the postoperative management. In the postoperative days hydrocortisone must be given intravenously to maintain blood pressure. The steroids should be continued for at least a week or 10 days during which time it may be cautiously withdrawn if conditions warrant. ACTH in stimulating doses is indicated during this period also to counteract the depressing effects of the hydrocortisone. It may be necessary to give small amounts of ACTH and prednisone over a considerable period of time until the patient is well stabilized.

Sedation during the emergency phases of an ulcerative colitis problem in the aged can be the source of severe problems but powerful drugs are not indicated as they may cause unfavorable reactions. Narcotics especially and drugs of the phenobarbital group also may react badly in older age patients.

Benadryl and Dramamine have been found to yield the most beneficial results and can be given intravenously or by intramuscular injection. The patient's reaction to a single dose of a drug must be carefully observed before repeating the medication. Usually the older age patients know what they can tolerate. Tranquilizers of the meprobamate class seem to be well tolerated.

Anticholinergics are of value only in so far as they reduce small bowel spasm and motility. Pro-Banthine has been the one most frequently used but caution is required regarding the presence of glaucoma. In any event before any anticholinergic is given inquiry must be made concerning the possibility of latent glaucoma or a severe problem in the eyes may be precipitated.

During all the problems arising from emergency situations in ulcerative colitis in the aged serious consideration must be given to the concomitant conditions such as diabetes, cerebral or cardiovascular renal complications.

In both the acute and subacute phases of ulcerative colitis in the aged one of the most serious and troublesome problems is that of rectal sphincter control. The cause for this is the inflammation in the distal segment involving the rectum and sigmoid. As a result of the disease in these areas there is constant straining, tenesmus and loss of rectal sphincter control.

The most efficient method of relieving this condition has been the intra-rectal instillation of 25 mg. (1 c.c.) of meticortelone acetate suspension in 30 c.c. of tepid tap water. The medication is placed in a funnel or irrigating syringe with a fine soft rubber catheter which is inserted into the rectum to just beyond the rectal sphincter. The fluid suspension is allowed to flow in by gravity. The patients usually are able to retain this medication from one to several hours and invariably state that it represents the first relief from their distress. They are usually unaware of the catheter or the small amount of fluid containing the medication. This treatment may be given once during the day and repeated at bed time but continued only for the time required to give relief of the symptoms.

Small stimulating doses of ACTH and prednisone are indicated in the acute or subacute exacerbations of ulcerative colitis in the aged. Usually 20 units of ACTH twice or three times weekly with 4 mg. of aristocort three times daily as a starting program will help control the problem. As soon as possible the amounts of steroids should be reduced so that a maintenance program of 10 units of ACTH weekly and 2 mg. or 4 mg. of aristocort once daily are all that are required.

The antibiotic and antibacterial agents are used both during the acute exacerbations and also as more or less maintenance dosages. The drugs most frequently used are chloramphenicol, carbarsone, diodoquin and erythromycin in rotation or in combination. Chloramphenicol in amounts of 1 gm. daily for at least a week or two is most valuable. It has been observed over a long period of years that small doses of carbarsone for one week a month only are helpful both in the acute phases and later on during the maintenance periods. The dose of carbarsone is 250 mg. three times daily for 7 days only and never repeated more frequently than at monthly intervals. It is to be remembered that this is an arsenical and even though mild is relatively nontoxic in the doses given. It does, however, have the potential of toxic reactions if administered in larger doses for more prolonged periods. There are only rare occasional patients who cannot accept this drug. The action of carbarsone seems to be quite nonspecific in ulcerative colitis even though it was originally introduced for the treatment of amebiasis. Carbarsone is occasionally used in combination with chloramphenicol or erythromycin but usually is given alone. Erythromycin may be given in an amount of 1 gm. daily to alternate with chloramphenicol. Diodoquin is usually given during the quiescent periods as a tablet of 0.6 gm. three times daily. It is antibacterial and its action is quite nonspecific but seems to help many patients to maintain an equilibrium and they feel improved.

Narcotics are contraindicated except in the very rare cases where pain cannot be otherwise controlled. During impending or actual perforation, or intestinal obstruction they must be given.

Diet is one of the most important phases of therapy in ulcerative colitis. It must be remembered that food is not the cause of ulcerative colitis, and also

that a single mouthful of food may cause a defecation reflex. It is possible to feed the ulcerative colitis patient with confidence. This individual requires more food intake than the average person because of loss of proteins and other valuable products through the bowel. Most patients tend to blame various foods for their ailments because they do not understand the simple principles stated above. The only real contraindications are alcohol in any form, coffee and highly spiced foods. So-called bulky foods are not harmful and actually if the patients like the taste of foods they are probably helpful. There is less pain and cramping when adequate amounts of foods of all sorts are taken.

Vitamins are allowed and actually urged. Many patients think they are sensitive or cannot take vitamins because of the peculiar odor when they belch or bring up gas. This is the natural odor of the vitamins and the patient should be urged to take them. Usually if taken with the meal there is less odor.

SURGICAL TREATMENT

The indications for surgical treatment include: 1. Massive or repeated hemorrhages which cannot be controlled. 2. Progressively downhill course in spite of all methods of therapy. 3. Intestinal obstruction. 4. A change from a mild to fulminating form of the disease with megacolon and evidence of impending perforation. 5. Carcinoma either with or unrelated to the ulcerative colitis.

Since the prognosis of ulcerative colitis in the aged is directly related to the age of onset, the older the patient, the more likelihood of his becoming a surgical emergency. Older age patients become debilitated at an alarming rate and one of the major problems is to evaluate the patient and give him the benefit of modern methods of surgical treatment before he is so depleted that he is too poor a risk for operation. Even though the patient in this age group may present surgical emergencies and in spite of the other problems of ageing, these situations can be met by prompt and careful teamwork between the surgeon, internist and anesthetist.

Hypothermia as an adjunct in anesthesia in these patients has proved itself to be most valuable by reducing the shock, and allowing for more rapid and precise surgical technic. Under hypothermia the whole prognosis of the surgical procedure is improved as shown by Cave and Bercovitz².

The depletion of adrenal cortical reserves in ulcerative colitis represents a serious medical management problem. In spite of what may appear as normal laboratory report for 17-ketosteroids these patients do not have enough adrenal reserve to carry them over the stress and strain of this disease especially if surgery is indicated.

In the postoperative periods especially close watch must be made of the calcium levels, proteins and electrolytes. Sufficient whole blood transfusions must be given until the hemoglobin, hematocrit and blood pressure are stabi-

lized. As long as adequate blood transfusions are given, there probably will be sufficient proteins available for the body use. There is, however, great tendency to give only fluids without adequate consideration of proteins and electrolytes especially potassium. If the total red blood cell count seems to be adequate but the protein and electrolyte balances not sufficient, then six months-old blood bank plasma or serum albumin may be given.

Many older patients apparently go through the initial phase of a surgical procedure and then suddenly go on to peripheral vascular collapse without any premonitory symptoms. This may happen at any time but most frequently develop from the second to the seventh days postoperatively. Unless adequate amounts of steroids are administered promptly intravenously the outcome may be fatal. It may be necessary to give up to 1,000 mg. of hydrocortisone in the period of a few hours to support the patient. At first there may be nothing more than a sense of not feeling well and no marked blood pressure changes.

Some older patients require small dosages of steroids postoperatively for considerable periods of time until they are fully stabilized. Usually a small stimulating dose of ACTH once or twice weekly will be adequate with a small daily dose of prednisone.

Early application of ileostomy bags are of prime importance. These should be applied at the time of operation. The new plastic bags have an adhesive surface on the ring and these are of great help in preserving the skin.

The type of operation which has developed over the years is total colectomy with abdominoperineal at the same time. Under hypothermia this entire procedure can be carried out with no shock to the patient. The ileostomy is usually handled with one of the cuff turn-back types of procedures.

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DISCUSSION

Dr. N. W. Chaikin (New York, N. Y.):—Dr. Bercovitz is to be congratulated for his timely and very informative paper. There is no doubt that we begin to see more and more nonspecific ulcerative colitis with onset in an older age group, and their clinical behavior is somewhat different from those of the younger age group.

There is very little that one can add to the therapeutic regime as outlined by Dr. Bercovitz except to emphasize that steroid therapy should always be

given cautiously in elderly patients. Our experience has been similar to that of Dr. Bercovitz, where a mild form of ulcerative colitis has assumed an acute fulminating aspect following steroid therapy.

It has been my impression that the onset of ulcerative colitis in patients in the 50's, 60's and upwards was infrequent. It should be pointed out that references in the literature to the incidence of onset of ulcerative colitis in the older age group is rather meagre. In a statement by Dr. Brust and Dr. Bargaen, they concluded that chronic ulcerative colitis among patients more than 60 years of age, although rare, may exist. A review of the literature on the incidence of ulcerative colitis in the elderly is given as between 3 and 21 per cent. In these reports, however, it is not entirely clear whether they are talking about the onset of the disease or the course of patients who have had the disease previously.

Our own experience comprises a group of 195 patients taken from three hospitals and private practices over a period of 12 years. In this group, we encountered 5 cases between 50-60, 2 cases between 60-70 and one over 70. It should be pointed out that, in evaluating our clinical material, no cases were included which gave a previous history of any functional colonopathy, ileitis, surgical intervention of any type, diverticulosis or diverticulitis.

Clinically, as Dr. Bercovitz pointed out, they may fall into one of three groups. Five of our patients: four between 50-60, and one between 60-70, presented themselves with a symptom-complex of diffuse, watery diarrhea, distention, abdominal pain, tenesmus, without any blood, mucus or pus in the stools. They presented difficult clinical and differential problems as well as therapeutic. The diarrhea was difficult to control, they usually ran a protracted course and convalescence was rather prolonged. Three of these patients have had a prolonged remission, one was subjected to surgery 2 years after onset because of diffuse hemorrhage, and one died of unrelated cause. Two patients presented themselves with severe rectal hemorrhage: one had to undergo emergency surgery and died postoperatively, while the other was controlled by conservative therapy. The patient in the 70's presented himself with an acute fulminating type of ulcerative colitis with blood, mucus and pus, and involvement of practically the entire colon; he died shortly after onset of the colitis.

In conclusion, from the above-stated remarks, it would appear that our experience differs statistically somewhat from that of Dr. Bercovitz. We had only eight cases out of 195 with onset after 50 years or approximately 4 per cent. The clinical picture as described by Dr. Bercovitz is similar to that which we have encountered where the onset was primarily that of watery diarrhea or hemorrhage. While it is difficult to draw any conclusion from our limited group, it would seem that ulcerative colitis in the older age group carries a more serious prognosis.

THE GRAVE PROGNOSIS OF ULCERATIVE COLITIS ENGRAFTED UPON ACUTE DIVERTICULITIS COLI*

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In the past five years a new clinical entity has been encountered, namely: the engrafting of acute, segmental, ulcerative colitis¹ upon instances of acute perforated diverticulitis of usually the distal, left sigmoid colon.

Sixteen such patients have now been encountered. Their treatment, because of their grave complications, has of necessity been surgical. Ten patients (62.5 per cent) died in the hospital. Careful search of the available medical literature has failed to locate previous contributions upon this subject—stressing the grave prognosis of this clinical syndrome.

Prior to 1955, our clinical experience with this alarming situation had been lacking. We have by now learned to regard this complication of diverticulitis coli with great apprehension. It is for this reason that it is believed desirable to report these few gravely ill patients, so that others may be on their guard and profit from our bad experiences.

A preliminary report² on this problem was made earlier in 1960. One thousand one hundred forty consecutive instances of acute diverticulitis coli have been similarly studied³ earlier this year. The reader is encouraged to study these two previous contributions for the sake of brevity and conciseness in this presentation. That data will *not* be represented in this contribution.

When a primary attack of segmental ulcerative colitis becomes subsequently engrafted upon a patient suffering with acute diverticulitis coli and its many complications, the prognosis in our limited experience, becomes most grave, with a rise in the ultimate mortality to about 62 per cent. Immediately, the surgical treatment picture changes, and *optimum* therapy calls for an immediate permanent ileostomy, a subsequent colectomy, and a combined abdominoperineal resection of the rectum and anus, as quickly as the patient's condition permits. In our limited experience with this rare complication, medical measures are valueless in preventing the spread of the acute ulcerative colitis with its consequent fistula formations, rapidly grave debilitation of the patient—which poses an actual threat to life, perforation with abscess formation, colonic lumen obstruction, and hemorrhage; even in defunctionated segments of the left half of the colon, in which the fecal stream has been entirely diverted away by a well functioning double-barreled transverse colostomy, and where daily irrigations of sterile saline and sulfasuxadine solutions were employed, but where *no* anti-

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biotics were used. Usually, these patients develop so many complications that you are never able to perform the optimum surgical treatment indicated, but must rather cope with enterocolic fistulas, paracolic and pararectalabdominal and/or perineal fistulas, abscesses draining through the anterior abdominal wall

TABLE I
DATA OF THIS STUDY

Case no.	Patient's initials	Sex	Age	Duration A.U.C. attack in days	Prev. A.U.C.	One-stage operation	Perforation	Fistula	Obstruction	Bleeding	Deaths
1.	S.E.R.	M.	38	43	none	yes	yes	no	yes	yes	no
2.	R.V.L.	F.	43	27	none	no	yes	yes	yes	yes	yes
3.	A.R.A.	F.	42	35	none	yes	yes	no	yes	no	no
4.	J.Q.B.	M.	45	16	none	yes	no	no	yes	yes	no
5.	M.R.T.	F.	46	23	yes	no	yes	yes	yes	no	yes
6.	S.T.J.	M.	40	17	none	no	yes	no	no	yes	yes
7.	J.W.McG.	M.	36	10	none	no	yes	yes	no	yes	yes
8.	R.M.S.	F.	37	15	none	no	no	yes	no	no	no
9.	D.V.L.	F.	40	21	none	yes	yes	no	yes	yes	no
10.	M.B.F.	F.	43	18	none	yes	yes	no	yes	no	yes
11.	A.B.N.	F.	44	22	none	no	no	yes	no	no	yes
12.	L.V.A.	M.	36	29	none	no	yes	no	yes	yes	yes
13.	G.J.S.	M.	40	34	none	no	yes	no	yes	no	no
14.	R.M.J.	M.	42	16	none	no	no	yes	no	yes	yes
15.	E.R.A.	M.	70	23	none	no	yes	yes	yes	yes	yes
16.	A.M.S.	F.	40	31	none	no	yes	no	no	no	yes
Totals: 16 patients.		F—8. M—8.	Aver. age: 42.62 years.	Aver. duration: 23.75 days.	One case	5 cases	12 cases	7 cases	10 cases	9 cases	10 deaths

and/or the perineum—vagina—or urinary bladder, profound hypoproteinemia, reversal of the A/G ratio, loss of potassium, profound and progressively worse secondary anemia, hemorrhage, failure of tissues to heal in a normal manner, and bacteremia.

Table I summarizes the salient facts in this study, in a brief and concise manner. It is self-explanatory.

Table II tabulates and compares the essential differences between this small series of 16 patients and 1,140 consecutive instances of acute diverticulitis coli. The comparison is thus facilitated by this means.

TABLE II
COMPARISON BETWEEN THIS STUDY AND 1,000 CONSECUTIVE CASES OF DIVERTICULITIS COLI

Condition	1,140 consecutive instances of diverticulitis coli ³	16 patients with A.U.C. engrafted upon diverticulitis coli
Patients over 40 years of age	95.2%	50.0%
Per cent of patients treated surgically	47.1%	100.0%
Abdominal pain with fever	53.2%	68.5%
Constipation	47.3%	12.5%
Diarrhea	34.6%	87.5%
Gross rectal bleeding	28.9%	56.25%
Colonic lumen obstruction	23.5%	62.5%
Localized perforation with abscess formation	25.4%	75.0%
Free perforation into peritoneal cavity	0.6%	0.0%
Colonic carcinoma and other rarer malignancies	3.2%	12.5%
Fistula formation	6.1%	43.75%
Palpable abdominal mass	31.4%	56.25%
One-stage operation 347 patients vs. 5 patients	34.7% (10 Deaths—2.88%)	31.25% (1 Death—20.0%)
Multistaged operations 148 patients vs. 11 patients	14.8% (12 Deaths—8.12%)	68.75% (9 Deaths—81.82%)
Sex	Females—48.3% Males—51.7%	Males—50.0% Females—50.0%

COMMENT

It is interesting to compare these 16 patients with a previously reported study³ of over 1,000 consecutive examples of acute diverticulitis coli. From

Table I, it is obvious that the ages of these 16 individuals is on an average far below that of the majority of persons suffering from diverticulitis coli (42.62 years, in the small group, as compared to 87.4 per cent over the age of 51 years, in the larger collection). The sex distribution was essentially equal in both series of patients. The incidence of perforation with or without abscess formation was 75.0 per cent (in the 16) as contrasted to 26.0 per cent (in the thousand), while that of fistula formation being 43.75 per cent (in the 16) as compared to 6.1 per cent. Colonic lumen obstruction occurred in 62.5 per cent (of the 16) as contrasted with 23.5 per cent (of the one thousand). Rectal bleeding was recorded in 56.25 per cent of the smaller group, and in 28.9 per cent of the large series. These 16 patients were found in 1,140 consecutive cases of diverticulitis coli, an incidence of 1.41 per cent.

From these comparative studies it would appear that the subsequent engrafting of acute ulcerative colitis upon acute diverticulitis coli greatly increased the incidence of complications and morbidity over that ordinarily encountered in acute diverticulitis coli. The mortality in 753 operations performed upon 485 individuals of the 1,000 patient group was 4.54 per cent as contrasted to 62.5 per cent in this small group of 16 persons.

The optimum therapy in examples of the engrafting of acute ulcerative colitis upon acute diverticulitis coli is a prompt total colectomy and proctectomy with a permanent ileostomy as a one-stage operation, only in those patients in optimum preoperative condition. Delay and temporizingly inadequate surgical procedures will result in disastrous grave complications and the probable loss of your patient's life. In this study, only five patients (31.25 per cent) were treated with the optimum one-stage operation, with a resultant death of one (20.0 per cent). The remaining eleven individuals (68.75 per cent) were of necessity treated by multistaged operations with nine deaths—a mortality of 81.82 per cent. In such a small group of 16 persons, the segregation of the multistaged operations into group procedures would have little statistical significance.

SUMMARY

1. Sixteen patients (1.41 per cent) were encountered in 1,140 consecutive examples of acute diverticulitis coli, that had an engraftment of acute ulcerative colitis upon their original colonic diverticular disease.

2. In comparing the two groups of individuals, the small aggregation of 16 persons showed the following by comparison: To be much younger in age, to have three times more colonic perforations with abscess formation, to possess seven times more fistula formations, to present two and one-half times more colonic lumen obstructions, to demonstrate twice as much frank rectal bleeding, to have 15 times more operative mortality, and only two-fifths as many were in optimum condition to permit a one-stage operative procedure.

3. Medical measures don't appear to offer too much hope of success in this group.

4. Only 6.25 per cent of these 16 individuals had had a prior attack of discernible acute ulcerative colitis.

5. In the present illness of these 16 persons, the average duration of the engrafting of their acute ulcerative colitis was 23.75 days previously.

6. The optimum therapy for these seriously ill patients is a one-stage total colectomy and proctectomy with a permanent ileostomy, if they can be gotten into satisfactory preoperative condition.

7. Less extensive surgical therapy is usually doomed to failure, with the frequent resultant loss of the patient's life.

8. The engrafting of acute, segmental ulcerative colitis upon a patient with acute, perforated, complicated diverticulitis coli, apparently from this inadequately small series of instances, seems to carry a grave prognosis, a high mortality, markedly increased morbidity, and requires definitive radical surgical treatment to restore health.

9. It is hoped that our unfortunate experiences may possibly aid others to improve upon our poor results and thereby save the lives of more patients in the future.

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DISCUSSION

Dr. Lynn A. Ferguson (Grand Rapids, Mich.):—When I received the letter asking me to discuss Dr. Collins' paper, I did not realize that we did have this unholy alliance occasionally, whereby colitis is superimposed upon an acute diverticulitis. I asked my resident if we had had any such cases and, after a little thought, he was pretty sure we had. I, therefore, asked our record department to pull the records on about 20 cases, if possible. They brought in about 60 records, but I did not have time to classify them very well, and threw out about 40. I wanted narrowed and shortened colons with acute episodes of colitis, and plenty of diverticula, so that I would have something to go by.

Dr. Collins cites a 62 per cent mortality. In my 20 cases, I did not have any deaths. In the other 40 that I had thrown out, I had 4. Actually, I think, we draw out material from, perhaps, 2 different sources. I know that he gets quite a number of patients from the County Hospital and, I believe, it boils down

to this. I am aware of the fact that we have all had moribund patients to mend who were distended and who had temperatures and, suddenly, it is up to the surgeon to do something about it. The patient has not been turned over by the internist in time, and I think that the gastroenterologists present here should take that to heart, and think it over, and let it sink in. When one is treating a case of ulcerative colitis, one needs a surgical consultant. As the patient gets worse, one has to have a little help. By the same token, we treat a considerable number of colitis patients in our hospital, and I do not waste any time in getting myself a good internist, as occasion arises. He is going to want a cardiograph, a chest film, blood chemistry, etc. As this patient gets worse, I like to broaden my shoulders by having the internist put a note on the chart. "I think this patient will take surgery". I do not believe that Dr. Collins has had this kind of help. I think his figures are a little high, however, when one stops to think that he picked 16 of these out of a thousand cases of diverticulitis, perhaps his figures are not so far off; maybe mine are. I think this situation calls for pretty good surgical judgment, and I like to play these cases by ear. I am pretty sure that Dr. Collins does the same. One tries to decide what is the minimum to be done to change the picture. These people, of course, have their electrolyte replacement taken care of; we know about their blood chemistry, etc., but they are pretty hard to boost back within a few hours. They usually have to be operated at the end of the day. Perhaps they come in in the morning in an ambulance, and something has to be done about it as soon as possible. There is, often, a perforation and that perforation must be diagnosed and drained. At least, they must usually have a proximal type of enterostomy. In general, I like to do a right transverse if the trouble is on the left side. The tic, however, may have to be drained retroperitoneally, through the flank. I like to open the abdomen, find it, and then decide what is to be done. I believe Dr. Collins would do the same.

It is easy to remove a colon and, in young individuals who have colitis, they are usually emaciated. One can usually do a colectomy and a proctosigmoidectomy in one stage, and do it rather easily. Diverticulosis, however, does not happen in young individuals very often. They usually occur in individuals who are fiftyish or past, and sometimes obese. This adds to the problem. They sometimes have hypertension and, perhaps, some type of heart disease of which the anesthetist is well aware and proceeds accordingly. The moribund patient presents a very grave problem. Good anesthesia, however, is a must under these circumstances. I feel a little more secure if the anesthetist has the patient intubated and on the re-breather. If necessary, the abdomen can be easily opened under local anesthesia and the procedure carried out with a fair degree of safety, but it does call for a little fast-moving teamwork.

I am very, very grateful to Dr. Collins for calling this to our attention, and I think perhaps most of us who have had experience along this line are aware that there should be more papers covering this unholy alliance.

Dr. H. B. Eisenstadt (Port Arthur, Texas):—I wanted to say about Dr. Collins' paper that we, of course, can in no way compare 16 cases with 354 cases. I am sure that if we got 350 cases of this combination we would have a better idea as to how serious this disease can be. My own experience with it is very limited. I am sure that Dr. Collins deserves credit for directing our attention to this combination.

I also think that I, as a medical man, would start to treat the patients more conservatively for a longer period of time unless it is absolutely proven that they will just go down in a very short time and I do not think it was proven that way. I would think that a plain colostomy on the right side, as Dr. Ferguson mentioned, or, at most, an ileostomy would be the maximum surgery that I would offer together with all kinds of medical treatment.

Dr. Frederick Steigmann (Chicago, Ill.):—What are the criteria of diverticulitis as put out by this group, and what are the criteria for regional ulcerative or segmental ulcerative colitis? We see very many cases of diverticulosis but diverticulitis, as we understand it, is comparatively not as common as one would take it from Dr. Collins' series. I work in a hospital where there are several thousand patients and I see patients in private practice too, but I see few cases of diverticulitis. As a rule there seems to be some difference of opinion among the radiologists and clinicians as to just exactly what diverticulitis is. Therefore, I would appreciate if Dr. Collins would give us his diagnostic criteria for both diverticulitis and segmental ulcerative colitis.

Dr. Henry A. Monat (Washington, D.C.):—I would just like to add that the paper of Dr. Collins and Dr. Ferguson's remarks were absolutely proper. I think I see quite a lot of ulcerative colitis being superimposed over diverticulitis. I would like to point out one thing in the treatment of the ulcerative colitis. Aside from the diets that are suggested and aside from the surgical management, liaison between the surgeon and internist is absolutely essential. During the quiescent period the patients ought to have psychotherapy, otherwise they may have frequent relapses in spite of all medical efforts.

Dr. Donald C. Collins (Hollywood, Calif.):—I wish to thank Dr. Lynn Ferguson very sincerely for his very fine discussion. I am certain that his cases and our type of patients are radically different. Most of our individuals were brought in by ambulance to the hospital. They come from a much poorer economic status, being neglected, without previous proper care, and reach us quite late in their disease. Since most of this report is derived from a county hospital practice, there is not the same speed in adequate definitive treatment that can be given to a patient under private hospitalization.

I wish to certainly highly compliment Dr. Ferguson on his 20 patients that he treated without a fatality. I think that record speaks volumes for the very fine surgical ability of Dr. Ferguson.

Dr. Ferguson and I see eye-to-eye on treatment. Each of these patients must be individualized in their proper care. In my presentation I described what constituted optimum treatment. This is the program we would like to follow, if possible. In most of these individuals, as Dr. Ferguson has so aptly said, you have to "play it by ear", having to gauge your surgical treatment to what your patient will stand and still be alive upon discharge from the hospital. As you will recall, there were only five of these 16 persons that we could treat in the optimum manner, performing a one-stage operation. There was just one death in these five individuals so treated. The remainder had many grave complications from the very start. These are the late examples that we as surgeons would appreciate seeing earlier.

To answer Dr. Eisenstadt: There were 1,144 consecutive instances of acute diverticulitis, and that constitutes one of the largest series in the literature at the present time. Yet, we only found 16 of these clinical entities. I can't add any other examples, since that's all there were. I agree with you that we should have more instances to report, but fortunately they are not encountered very often.

What I desired to emphasize before this fine group this afternoon, is that these clinical syndromes are potentially "dynamite" and are equally as dangerous to the gastroenterologist caring for them. Just like the villous-tumors of the anorectum, that you are familiar with, gentlemen. You may have a patient with one of these lesions in apparently fairly good health, and yet he may be dead three days hence from unrecognized acute electrolyte loss, unless energetically treated. Unfortunately, some doctors fail to recognize these tumors and are at a loss to explain the sudden failure and death of their patient. Thus, there are certain acute surgical emergencies that we have to treat correctly with an absolute minimum of delay. I am indeed sorry that we didn't have more individuals, Dr. Eisenstadt.

To answer the questions as to how we made our diagnoses: the diagnosis was made by very competent internists and radiologists. It was based upon the patient's history and physical findings, comprehensive laboratory tests, and adequate roentgenologic studies. These represented very acute instances of acute diverticulitis. There were no subacute nor chronic individuals included in this report. These were so diagnosed by some of the most competent medical authorities in Los Angeles.

I wish to compliment Dr. Monat for his very fine discussion and I desire to sincerely thank all the discussants for their excellent help in this problem.

CARCINOMA OF THE COLON*

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Among the visceral neoplasms affecting man, cancer of the colon ranks high in frequency and in curability. Recent studies indicate that even better results might be obtained from surgical therapy if all the known facts concerning this disease are borne in mind. The present paper is based on our experience with 1,000 operations for cancer of the colon over the past 20 years and outlines the present concept for surgical management of this disease.

Preoperative preparation:—The advent of antibiotics which made sterilization of the bowel feasible, revolutionized colon surgery. By minimizing the danger of infection and peritonitis more radical resections with primary anastomosis became routine and the mortality and morbidity of colon resection comparable with that of other abdominal operations. More recently the emergence of resistant organisms and secondary invaders in the sterilized colon has prompted review of the problem of antibiotic preparation for surgery and it has become clear that "routine" preparation is inadequate and preliminary culture and sensitivity studies are essential. This can best be done by determining the antibiotic sensitivity of a mixed suspension of stool organisms and tailoring the preoperative medication to fit¹. We have found that in so doing we have reduced the incidence of complications caused by infection². It has become apparent that as antibiotics become more popular and more widely used they become less effective and resistant organisms more frequent.

A mechanically clean bowel is essential for accurate surgery and this is accomplished by a fluid low residue diet, daily colonic irrigations and catharsis for 48 hours prior to surgery. It is mandatory that obstruction of the colon, whether partial or complete, be relieved before definitive surgery. This may often be accomplished by intubation and enemas but in some instances a preliminary decompression procedure is necessary. A simple loop colostomy in the transverse colon is the preferred operation for all lesions in the sigmoid and descending colon. This effects complete diversion of the fecal stream and is a useful safeguard for subsequent resection and anastomosis. In cases where the cecum is markedly enlarged by x-ray, cecostomy is preferred because of the danger of performing a transverse colostomy and missing a perforation in the cecum. In these patients the cecum is exteriorized so that an effective vent is produced.

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The preoperative correction of anemia, nutritional deficiencies and fluid and electrolyte imbalance has helped to reduce the mortality of colon surgery. Since many patients are in the sixth and seventh decades and suffer from degenerative diseases it is important to protect them from cardiac, respiratory and urinary complications and to be aware of any other associated conditions.

Careful attention to the details of preoperative management will be rewarded by increased technical ease and a smoother postoperative course.

Operative procedure:—As experience has increased a more radical approach to the resection of lesions of the colon has gradually evolved.

In all patients in whom a curative resection is carried out the following points are routine:

1. Thorough removal of lymphatic drainage areas with high arterial ligation and wide resection of posterior peritoneum and retroperitoneal tissues in the region of the lesion.

2. Occlusion of the bowel lumen above and below the lesion to minimize intraluminal spread of desquamated cells which may become implanted in the line of anastomosis.

3. Early ligation of the veins draining the area of the lesion to prevent dissemination by venous emboli during manipulation of the tumor. We have found that the number of viable tumor cells in the venous blood is increased during surgery and at present are studying the effect of intravenous nitrogen mustard during operation in killing these cells in their most susceptible phase. It appears likely that the use of some intravenous tumoricidal drug may become a routine part of all resections for cancer.

4. Extensive resection of colon, subtotal colectomy, in all patients in the younger age group in whom the operation is thought to be curative. Limited resection is reserved for bad risk patients, for palliative resections and for those individuals whose long term prognosis is doubtful because of associated disease.

This viewpoint has arisen from a study of our own material. In 450 patients undergoing colon surgery for cancer, 27 (6 per cent) ultimately developed a second primary lesion. Because of the fact that many patients died within a year of operation owing to metastatic disease or to associated degenerative conditions we felt that this figure did not represent a true incidence and when we excluded all patients who failed to survive five years, the incidence of second primary tumors increased to 15 per cent. To test this concept further we routinely performed a subtotal colectomy to the level of the rectosigmoid in a group of 100 patients with carcinoma of the colon. This was done to determine the actual incidence of adenomatous polyps, the frequency of malignant change and to assess the more radical procedure in terms of mortality and morbidity. The results of this study are interesting.

In this group, 40 patients had multiple (more than three) adenomatous polyps associated with a single carcinoma and in eight cases malignant change was present either as a frank carcinoma or malignant degeneration in a polyp. Three of these second malignant tumors were palpated in the colon; the remaining five were unsuspected until the specimen was examined by the pathologist. It would appear that many of the so-called second primaries of the colon are present at the time of resection of the first lesion and are unrecognized until months or years later when they produce clinical symptoms or grow large enough to be demonstrated on barium enema.

The operative mortality in the original group was 9 per cent. This was the same as in a comparable group of city hospital patients subjected to a more limited resection. In the author's personal series of 89 subtotal colectomies for cancer of the colon there has been one operative death. The only postoperative problem related to the increased extent of resection is frequency of bowel movement. This occurs initially in all patients but is temporary (2 weeks to 2 months) except where a long segment of terminal ileum has been removed. Postoperative x-ray studies in this group demonstrate that the terminal ileum becomes hypertrophied and colonic in appearance and apparently takes over the water absorbing function of the large bowel.

From this experience we are convinced that multiple polyps of the colon frequently accompany clinical carcinoma and that second primary lesions may be present in a fair percentage of cases. In younger individuals in whom the operation is considered curative a more radical resection is indicated; the entire colon to the level of the rectosigmoid should be excised. Limited resections are reserved for poor-risk patients, for palliative operations and for patients whose long-term prognosis is doubtful because of associated disease³.

Postoperative management:—The principles of postoperative care have been established as follows:

1. Decompression of the intestinal tract by intubation until peristalsis returns. This may be accomplished by nasal intubation or by direct insertion of a catheter into the bowel through a stab wound. The latter method is useful in older patients in whom prolonged intubation may be necessary⁴.
2. Antibiotic coverage guided by the preoperative stool cultures.
3. Replacement of blood, fluids and electrolytes.
4. Careful attention to tracheobronchial toilet. Pulmonary complications are a major source of morbidity and mortality and in most instances are caused by aspiration or accumulation of secretions.

Results of surgery:—In the past 20 years we have had the experience of dealing with 1,000 cases of carcinoma of the colon. Statistics for the group as a whole are meaningless because of changes in operative technic and improve-

ments in pre- and postoperative management. The concept of treatment outlined in this paper has been in effect for six years and has been applied to 340 patients. In this series there have been 14 deaths, an over all mortality rate of 4.1 per cent. In 89 patients a radical subtotal colectomy has been carried out as a curative operation with one surgical mortality. This is admittedly a selected group since all of these patients were under 70 with no associated disease and no dissemination of carcinoma. This series is too small for statistical analysis and the follow-up is short but to date we have seen no early recurrences and it is our hope that the ultimate results will be improved.

SUMMARY AND CONCLUSIONS

The experience gained from the surgical treatment of 1,000 cases of carcinoma of the colon has led us to the following conclusions:

1. Preoperative sterilization of the bowel contents is essential and must be controlled by antibiotic sensitivity studies.
2. Operative procedures must be designed to prevent dissemination of tumor cells through the lymphatics and veins and via the intestinal lumen.
3. A more radical resection of the colon will reduce the incidence of second primary lesions.
4. Careful long-term follow-up studies and autopsy reports on all patients dying following resection for carcinoma will ultimately prove or disprove the validity of these observations. This material is presented at the present time as a preliminary report.

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PALLIATION IN THE MANAGEMENT OF CARCINOMA OF THE COLON AND RECTUM*

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Carcinoma of the colon and rectum has a more favorable prognosis than carcinoma in any other portion of the gastrointestinal tract¹. In early cases when no lymph nodes are involved the five-year survival rate approaches 75 per cent^{2,3}. When nodes are involved the five-year survival rate is approximately 35 per cent. Little improvement in these figures can be expected by extending the scope of surgery or doing radical pelvic and abdominal lymphadenectomies⁴. This has been done by several groups with an increase in complications and hospital morbidity and only a questionably significant improvement in the five-year survival rate^{3,5}. It is not recommended as a routine procedure.

Until more is known about cancer and until other methods of treatment are developed, we must continue to manage carcinoma of the colon and rectum as we currently do. The only immediate improvement obtainable in the results of treatment of carcinoma of the colon and rectum is by diagnosing the disease earlier. The difference between a five-year survival rate of 75 per cent and 35 per cent, depending upon nodal involvement, is mute evidence of the importance of early diagnosis. At present delay in the diagnosis occurs in eight out of ten cases⁶ and this delay averages over six months⁷. The physician is responsible for delaying the diagnosis in 31 per cent of patients with carcinoma of the colon and rectum; one-half of the physicians causing this delay are qualified specialists⁸.

The National Cancer Institute⁸ has estimated that only 15 of every 100 patients with cancer of the rectum are being cured, whereas early detection could cure 70. The first physician seen by the patient following the onset of symptoms very often determines whether a carcinoma of the colon or rectum is cured or whether it kills the patient⁹.

In our current management of this disease palliation unfortunately plays the leading role. The 75 per cent five-year survival rate in early cases mentioned above is excellent, but it involves only a small number of patients in whom the diagnosis is made. In a review of 330 private patients, I found that 22 were not submitted to surgery as the disease was obviously terminal. A palliative resection or some palliative surgical procedure was done on 76. In the remaining 232 cases I resected the lesion as a curative procedure.

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If we consider 100 patients on whom a diagnosis of carcinoma of the colon or rectum has been made, 7 will be beyond surgical help, 23 will have a palliative surgical procedure done, 70 will have a resection with hope of cure, 3 will die following operation, and 33 will be alive five years later. Other studies indicate only 25 will be alive 5 years later⁹ (Fig. 1).

It is the purpose of this paper to discuss palliative measures that can be helpful as well as harmful to approximately 67 per cent of patients with carcinoma of the colon or rectum who eventually look to us for some help or hope.

Before any palliative measure is instituted it is most important that two things be definitely determined; first, are we positive that some curative operation still could not be done, and secondly, just what are we attempting to accom-

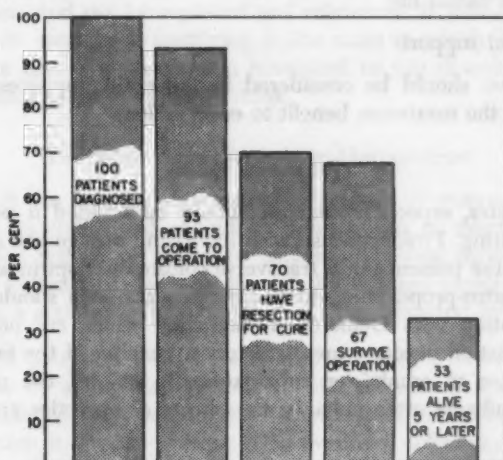


Fig. 1—Expectation of survival of patients having carcinoma of the colon.

plish. A careful and thorough examination must be done to determine the location and extent of malignant involvement before these two basic questions can be answered. Carcinoma of the colon with extensive local involvement of adjacent pelvic or abdominal organs frequently is still in a curative stage if it is removed¹⁰. Even recurrent carcinoma does not mandate palliative treatment *a priori*. Over 40 per cent of recurrent carcinomas of the colon and rectum can be resected again, and one-third of these patients will be alive 5 to 16 years later¹¹. If any doubt exists as to re-resectability, the patient should have the benefit of exploratory celiotomy.

When nothing curative can be attempted a positive approach to the problem of palliation must be maintained. When the physician adopts a negative attitude, the patient suffers. Merely renewing a narcotic prescription is not proper pallia-

tion. Too often the busy surgeon loses interest because there is nothing more to cut, and the internist is not interested in taking over the terminal care of a hopeless surgical case. It might be well at this point for both to recall the aphorism of Edward Trudeau, "To cure sometimes, to relieve often, to comfort always".

What are we attempting to accomplish by palliation? This question must be asked and answered for each patient. If it is not asked and answered carefully, unnecessary suffering by neglect or unnecessary operations and colostomies will follow. Palliation can accomplish four things only:

1. relieve pain
2. prevent or relieve obstruction
3. prolong a useful life
4. give moral support

All four objectives should be considered in preventing unnecessary treatment and in obtaining the maximum benefit to each patient.

RELIEF OF PAIN

Drugs:—Opiates, especially codeine, should be avoided if possible as they are very constipating. Prolonged use with increasing dosage can cause fecal impactions even in the presence of a transverse colostomy. Aspirin and nonnarcotic drugs such as dextro-propoxphene-hydrochloride (Darvon) should be used first, later in combination with Demerol or methadon which are not constipating. When oral medication becomes unsatisfactory a member of the family often can be instructed how to administer subcutaneously one of the nonconstipating narcotics. Tranquilizers often enhance the effects of narcotics and allay apprehension.

Cordotomy:—Section of the anterolateral pathways of the spinal cord occasionally is necessary for the relief of severe pelvic, perineal, or leg pain. Such pain is the result of pelvic recurrence following resection of a rectal carcinoma. Abdominal visceral involvement may be absent and a useful, pain-free life can be extended by cordotomy. It should be done before undue suffering and debilitation have ensued. Turnbull¹² has called attention to the tendency to postpone cordotomy when it is indicated and has been considered.

Prefrontal lobotomy:—Section of the frontal thalamic fibers can be done easily under local anesthesia. It is a less formidable procedure than cordotomy and should be considered in carcinomatosis when pain cannot be controlled by drugs. The absence of pain and the altered attitude affords relief to the patient and his family.

Radiation therapy:—X-ray or interstitial radiation frequently will relieve pain from metastases arising from carcinoma of the colon or rectum. Henschke¹³

reported symptomatic relief in over half of the patients so treated. Palpable masses may become smaller for a prolonged period. Mayo¹⁴ reported a 20-year survival following palliative radiation therapy for inoperable carcinoma of the rectum. Wise and Smedal¹⁸ reported relief of pain by use of two million volt radiation.

Hypnosis:—Only the uninformed physician believes that hypnosis is akin to black magic¹⁶. Amazing results are possible with hypnosis in relieving pain, reducing or eliminating narcotics, and changing the attitude and outlook of patients with carcinomatosis. These unfortunate individuals have a strong motivation to obtain some measure of relief and they respond readily to hypnosis. Old or senile individuals are not induced easily, but intelligent, alert patients can be put into a hypnotic state in one or two minutes. The posthypnotic suggestions are given and can be repeated and reinforced at subsequent sessions as necessary. Results have been gratifying in the cases in which I have used hypnosis during the past two years. I am convinced its use should be expanded in managing terminal cases of carcinomatosis.

PREVENTION AND RELIEF OF OBSTRUCTION

Resection of the primary tumor in the presence of metastases that cannot be removed is justifiable and should be done unless so much of the liver is involved that the procedure would be useless. Five-year survivals occurred in 15 per cent of patients having resection of the primary tumor in the presence of metastases in a series of 175 palliative operations reported by Swinton, et al¹⁷.

Experienced judgment must be exercised to prevent cecotelic operations¹⁸. In the presence of widespread hepatic or visceral metastases a colostomy to prevent obstruction should not be done unless there is definite evidence that clinical obstruction is already present. A "preventive" colostomy brings unnecessary suffering to the patient and his family. A low residue and later a nonresidue diet should enable the patient to complete his stay in relative comfort¹⁴. In the rare case where complete obstruction later ensues, a loop colostomy might be necessary. Small bowel obstructions from adhesions or metastases have occurred above a "preventive" colostomy while actual occlusion of the lumen of the colon never occurred. A "preventive" colostomy is an unnecessary colostomy.

Side-tracking procedure such as ileocolostomy or colocolostomy around lesions that cannot be locally resected can be done easily with great benefit to the patient. Obstruction is prevented without an abdominal colonic stoma.

Rare occurrences of disappearance of a large, nonresectable, obstructing carcinoma of the colon after a palliative colostomy have been reported^{19,20}.

Fulguration:—Occasionally fulguration is useful as a palliative measure in keeping the lumen of the rectum patent in elderly patients. It can be used to

reduce the bleeding and the secretion of mucus when the lesion cannot be excised locally.

Case 1:—Examination of a feeble, decompensated 79-year old male revealed a carcinoma of the anterior rectal wall 4 cm. in diameter located 6 cm. above the anus. His cardiac status precluded any surgical procedure. The lesion was fulgurated periodically for four years until he expired from a heart attack.

Case 2:—An active 85-year old woman with pulmonary metastases from bilateral carcinoma of the breasts complained of profuse rectal bleeding. Examination and biopsy revealed a small actively bleeding adenocarcinoma of the anterior rectal wall. She refused to enter the hospital for local excision so the lesion was fulgurated. Three months later a small nodular recurrence at the same site was fulgurated. She is alive without rectal bleeding 9 months later.

PROLONGATION OF A USEFUL LIFE

When properly employed all the aforementioned procedures can aid in prolonging a useful life. Life *per se* may not be prolonged, but a useful, more comfortable life can be extended. Exenterations and radical surgical procedures for metastases from carcinoma of the colon and rectum increases the suffering of the patient and prolongs the period of hospitalization. It is extremely doubtful if it prolongs life. Fansler²¹ has stated that when palliation is the object of treatment, simple procedures will give the patient more comfort and as many years of life as exenterations and similar radical procedures. Transfusions, infusions and heroic measures during the last few days or hours will not prolong a useful life and often add to the patients suffering.

Palliative efforts to prolong a useful life by chemotherapeutic agents has not been demonstrated. Many agents are being investigated currently, but their use should be restricted to carefully controlled studies. Perfusion of pelvic organs with these agents by means of a heart pump and oxygenator are fascinating studies, but are not applicable clinically at this time^{22,4}.

SUPPORT OF PATIENT MORALE

The fourth objective of palliation, support of the patient's morale, will be achieved by the physician's earnest efforts to achieve the other three objectives. If something is being done, regardless of results, the patient's outlook will be helped. Hope springs eternal, and even when the patient realizes his plight, he still hopes. To be seemingly abandoned and alone is a despairing dilemma and forces some terminal patients or their families to seek aid from unscrupulous sources. If the physician or surgeon is interested in diagnosing and treating patients with early malignancy, it is his responsibility to help them in the late stages of the disease. Even a show of interest and talking to the patient will

help. Kipling is credited with saying that words are the most powerful drug used by mankind.

SUMMARY

Palliative treatment is necessary in approximately 67 per cent of patients in whom a diagnosis of carcinoma of the colon or rectum is made. Extending the scope of surgery will not improve this figure. Decreasing the current 80 per cent delay in the diagnosis of the disease should increase the number of patients surviving five years.

Before palliative measures are instituted it must be definitely determined that a curative procedure still could not be done. In case of doubt exploratory celiotomy is indicated.

When the patient is beyond the curative stage there is still much that can be done if the physician takes an active interest and assumes a positive approach to the problem. The results are often rewarding with survivals beyond 5 years not uncommon.

Four things can be accomplished by palliation: relief of pain, relief or prevention of obstruction, prolongation of a useful life, and support of the patient's morale. Before the patient is subjected to possible additional suffering from any palliative measure, the possibility of accomplishing these objectives should be weighed carefully.

Palliative exenterations and similar radical palliative procedures have little to offer in prolonging the patient's life and relieving his pain. A "preventive" colostomy should not be established in the expectation that obstruction might develop at some time in the future. A "preventive" colostomy is an unnecessary colostomy.

When properly and sensibly employed, drugs, diet, radiation, fulguration, hypnosis, and surgery have much to offer as palliative measures in the management of carcinoma of the colon and rectum.

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DISCUSSION

Dr. Milton J. Matzner (Brooklyn, N. Y.):—I wish to congratulate both authors on their well prepared papers. I would like to make a few comments first about Dr. Ripstein's presentation. He covered the subject in an interesting and thorough manner. There are some thoughts I feel should be re-emphasized and a few additional comments seem worthy of expression.

As stated by Dr. Ripstein, the proper use of intestinal antisepsis has revolutionized colon surgery. The importance of a mechanically clean bowel has likewise been stressed. He made some comments about the routine preparation, stating it was perhaps somewhat inadequate and he felt preliminary culture and sensitivity studies are essential. It is of interest that Dr. Poth recently commented in the June 1960 issue of the *Journal of Surgery* that the combination of neomycin and sulfathaladine is a very effective combination and did not give him or his colleagues any adverse complications.

I would appreciate some comments by Dr. Ripstein concerning his comparative experience with this combination, particularly because I felt that in

some instances it may not be feasible to delay for 36 hours until these sensitivity studies are completed and then to begin the therapy for intestinal antisepsis as outlined in his presentation.

In the author's comments about a curative resection he emphasized the occlusion of the bowel lumen above and below the lesion to minimize intraluminal spread of desquamated cells which may become implanted in the line of anastomosis. In this regard, Cole has also emphasized recently the hazard of implantation and survival of malignant cells which might well be augmented by intestinal antiseptics by their production of the medium essentially void of bacteria. I would appreciate if Dr. Ripstein also would comment on his experiences with the use of diluted Dakin's solution as an irrigant in the lumen of the bowel in preventing tumor implantation and transplantation.

As experience has increased, the more adequate and complete approach to curative resection of colonic neoplasms has been widely adopted. In the post-operative management program, the modern recovery room has also been invaluable.

With regard to Dr. Remington's paper, I feel that he has presented his subject very concisely and he has aptly stated that until more is known about cancer and other methods of treatment are developed, we must continue to manage carcinoma of the colon and rectum as we currently do. Based on my observations as a gastroenterologist, I wish to re-emphasize that improvements in the results of treatment of carcinoma of the colon and rectum may be anticipated by diagnosing the disease earlier. This will necessitate the prompt recognition of warning symptoms and the performance of necessary examinations. Among these should be included stool examinations for blood, digital and proctosigmoidoscopic investigation of the lower bowel, the employment of modern radiographic technics and, where facilities permit, exfoliative cytology study of the colon contents. To this one should add the earlier detection and destruction of precancerous lesions.

Although the ultimate aim of all operations for cancer is cure, there is nevertheless a definite group of cases which are inoperable and of necessity require palliative procedures.

Dr. Remington has well stated that palliation can accomplish four things and probably only four things: one, the relief of pain; two, prevent or relieve obstruction; three, prolong a useful life; and, four, give moral support.

Our limited experience with chordotomy for relief of pain has not been a successful one. Cobalt therapy of pelvic lesions has frequently produced untoward symptoms. Its effectiveness has been somewhat better with bony and pulmonary metastasis.

It is important to re-emphasize that a preventive colostomy is an unnecessary colostomy. We also feel that advanced obstruction is the only indication for colostomy.

We have had no experience with hypnosis as a palliative measure, although I have spoken to some surgeons in my area and one in particular stated he too has found it to be of some help in utilizing posthypnotic suggestion.

Limited experience with isolation perfusion of pelvic organs with chemotherapeutic agents has not been sufficiently beneficial up to this time for palliation. We have found that a well organized tumor board with representatives of many services of the hospital has been useful in the re-evaluation of the patient's problems that frequently have arisen postoperatively and have frequently been of significant service in improving our program of palliation.

I would again like to thank the authors for the opportunity to discuss their papers and compliment them on their presentations.

Dr. C. B. Ripstein (Brooklyn, N. Y.):—I would like to thank Dr. Matzner for his excellent discussion.

In regard to the questions he has asked, we agree that neomycin and sulfa-thalidine, or any of the sulfa derivatives, is probably the best routine preparation and in those cases where there is urgency for early operation we utilize it too. We have, however, found that a certain percentage of individuals will show organisms, pathogenic organisms, that are not affected by even this combination. Nothing is 100 per cent successful, and I think it makes more sense to individualize the preparation of the bowel wherever feasible.

We have not used Dakin's solution to irrigate, and, incidentally, although it's not a commercially beneficial statement, Dakin's solution is exactly the same as chlorpactin which has been advertised as an effective therapeutic agent in tumors. There is no difference whatsoever. We have not used it because we are very anxious to estimate the value of our prophylactic adjuvant therapy in using thiotepa. We want to use local recurrences as one indication of its value, so we do not want to confuse the picture at the present time, but I think if you are going to overcome this difficulty that it might be a useful addition to therapy.

STUDIES OF SYSTEMIC HEMOSTATIC FACTORS IN PATIENTS WITH BLEEDING DUODENAL ULCER*

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During the course of studying the clinical use of glycerolized frozen blood at the United States Naval Hospital in Chelsea, Mass.¹⁻³, under the joint supervision of the Department of the Navy and the Protein Foundation of Boston, Mass., it was surprising to find no reports of comprehensive studies of *systemic hemostatic* factors in patients with duodenal ulcers, with or without evidence of bleeding. Many other factors have been recently re-emphasized, notably local ones affecting the hemostasis in bleeding duodenal ulcers, e.g.: inflammatory changes in vessels⁴, as opposed to previously stressed importance of arteriosclerosis (and hence age)⁵, salicyl compounds⁶, which is disputed by certain authors⁷ who are in the minority.

But by far the most penetrating, comprehensive and meticulous study, both *in vivo* and *in vitro*, on local environmental factors affecting hemostasis in bleeding from the upper gastrointestinal tract was carried out by Bodi, Wirts, and Tocantins and reported in the 1956 edition of *Progress in Hematology*, edited by Dr. Tocantins⁸. It is beyond the scope of this paper even adequately to summarize here the many variables considered and all the contributions in this study. Suffice it to mention two of the most significant findings stressed by the authors themselves: 1. Gastric juice buffered with a large dose of aluminum magnesium hydroxide mixture markedly reduced clot lysis, which coincided with minimal or absent peptic activity; 2. posthistamine gastric juice consistently prevented clotting of blood when mixed in equal portions and fasting gastric juice usually delayed or prevented it, but these effects could be obviated by

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buffering with milk, cream, a milk and cream mixture, a milk protein preparation, and antacid gel.

This investigation was first prompted about one year ago following the adoption of more comprehensive and practical battery of screening tests for bleeding disorders, including the highly sensitive partial thromboplastin test⁹ in connection with the aforementioned Blood Research Project³; our Residency Training Program; after the additional use of a well-standardized oral ascorbic acid saturation test¹⁰ in certain originally poorly understood bleeding disorders¹¹; after review of some of the more voluminous pre-World War II literature on experimental scurvy in guinea-pigs (20 of 75 developed peptic ulcers versus none in 1,000 controls)¹², and in an initially "normal" human being (without evidence of peptic ulcer before or during the experiment)¹³, and particularly clinical and laboratory studies indicative of high incidence of "subclinical scurvy" in patients with peptic ulcers¹⁴⁻¹⁸ and especially bleeding therefrom¹⁹⁻²¹.

It is believed in retrospect that it was perhaps fortunate that, prior to beginning the study, we had not read the scholarly "Medical Progress" paper entitled the "Physiologic Significance of Vitamin C in Man" published in 1944 by Pijoan and Lozner²². They were so critical of the previously held widespread concept of subclinical scurvy and presented arguments so plausible at that time, against the validity of sporadic low or negative blood, plasma or urine levels of ascorbic acid and even the oral or intravenous saturation tests, that this at least *appeared* to have had a stifling impact on further studies in this direction, judging from the paucity of pertinent reports during the subsequent 12 years, e.g.^{23,24}. Their reasoning then—though less potent *now* in the face of much direct and indirect new knowledge acquired since then—might almost have been enough to have dissuaded us(!) from combining our studies of ascorbic acid with commoner and more conventional screening tests for "bleeding disorders" in the following investigation of duodenal ulcer.

MATERIALS AND METHODS

The study was limited to patients with radiographically confirmed duodenal ulcer, with or without hemorrhage, either gross or occult, and with one exception, without coexisting frank symptoms or signs of other disorders commonly designated as arterial, endocrine, or "hemorrhagic" or deficiency diseases. It did not include those with concomitant parenchymal liver or biliary tract disease, in which systemic hemostatic defects have been found, often multiple and highly complex (as many as 16 possible defects identified)²⁵. It also did not include patients developing ulcers in the course of steroid or salicylate therapy or the administration of other drugs suspected of being ulcerogenic or of causing blood dyscrasias.

The first 10 cases (Group I) selected for study had the usual complete blood count, hemoglobin, hematocrit, gastric analysis with guaiac test, serial

stool guaiac tests, as well as platelet counts by the direct method with phase microscopy²⁸, Lee-White clotting time, "prothrombin time" by the one-stage Quick method, bleeding time (Duke technic, usually in both ear lobes) and a tourniquet test with the Rumpel-Leeds technic. The incidence of abnormal or borderline results in even these few cases was sufficient to prompt their repetition in a number of instances, to improve the technic and care with which they were done, and to expand our screening tests for hemostatic defects.

The next 7 cases (Group II) had two additional tests, namely—the partial thromboplastin time and the ascorbic acid saturation test. One of our technicians (C.A.D.) was taught the former in a local laboratory⁹ which has had considerable experience in the procedure^{27,28}.

TABLE I
HEMOSTATIC FACTORS IN ACTIVE DUODENAL ULCERS

	Group I 10 cases	Group II 7 cases	Group III 10 cases	Total cases (27)	No. cases with 1 or more hemo- static defects
Recent gross hemorrhage	1	4	3	8	6
Recent occult hemorrhage	7	1	7	15	12
No physical or chemical evidence of recent hemorrhage	2	2	0	4	1*

*See text for details of this case.

The technic of the partial thromboplastin test is as follows: Blood is drawn by letting 4.5 ml. drip from a siliconized needle into a siliconized tube with 0.5 ml. of sodium citrate, 0.1 M as an anticoagulant. The specimen is inverted once and immediately put into an ice bath and then spun at approximately 3,500 rpm for 20 minutes while packed in ice. Three immaculately clean Kahn tubes are placed in a 37°C. water bath. Four ml. of calcium chloride 0.03 M are pipetted into a test tube and also placed in the 37°C. water bath. A 1:1000 dilution of brain cephalin is made by pipetting 0.1 ml. of thawed brain cephalin in a 100 ml. graduated cylinder and diluting to volume with 0.85 per cent sodium chloride solution. With a clean 1 ml. pipette 0.1 ml. of the dilute brain cephalin and 0.1 ml. of plasma are pipetted into each of the three Kahn tubes. The tubes are allowed to incubate for 5 minutes to come to the temperature of the water bath. One-tenth ml. of the 0.03 M calcium chloride that has been in the water bath is blown into one of the Kahn tubes and a timer started at the same time. The specimen is slowly agitated with a platinum loop until a clot

forms. After the earliest stages of learning this method about 10 months ago (January 1960) excellent reproducibility has been achieved in this laboratory. Normal values have been considered to be from 70 to 100 seconds. It is important, however, that all glassware used in this procedure be scrupulously clean and that the same type of pipettes be used throughout the procedure.

The second screening test mentioned above and not ordinarily included for "hemorrhagic disorders" was the oral ascorbic acid saturation test. The procedure as used at the Massachusetts General Hospital¹⁰ is as follows:

The patient voids (usually on arising in the morning) and discards his urine; 2 hours later he voids completely again, and collects the urine as the control specimen. At this time he ingests a loading dose of 500 mg. of ascorbic acid; 2 hours and 4 hours thereafter the 2nd and 3rd specimens are collected.

All 3 specimens are analyzed according to the following method based upon those of Roe and Kuether²⁰ and Shaffert and Kingsley²⁰, viz: One ml. of urine is added to 19 ml. of 4 per cent trichloroacetic acid along with one-half teaspoonful of Norit activated charcoal and shaken vigorously for one minute in order to oxidize the ascorbic acid to dehydroascorbic acid (reversible oxidized ascorbic acid). A filtrate is obtained by filtering through Whatman No. 42 filter paper. Four ml. of the filtrate are treated with one drop of 10 per cent Thiourea solution and 1 ml. of 2 per cent 2,4-dinitrophenylhydrazine. The 2,4-dinitrophenylhydrazine forms and hydrazone and the thiourea prevents interference by oxidizing substances such as Fe^{+++} and H_2O_2 , which also produce a color with 2,4-dinitrophenylhydrazine. The tubes are placed in a boiling water bath 10 minutes and then placed in crushed ice for 5 minutes. Five ml. of 85 per cent sulfuric acid are added to each tube, drop by drop, and the tubes mixed by twirling. The strong sulfuric acid produces a red color. Each specimen is read in the Coleman Jr. Spectrophotometer at a wavelength of 540 milimicrons against its own blank, which was prepared in exactly the same manner, except for the omission of the 2,4-dinitrophenylhydrazine until after the addition of the sulfuric acid.

A standard solution of reagent grade l-ascorbic acid containing 30 mcg. per 1 ml. is prepared and analyzed along with each group of unknowns. The results are calculated according to the following formula:

$$\frac{\text{OD (unknown)}}{\text{OD (standard)}} \times 0.03 \times \frac{\text{volume}}{0.2} = \text{mg. ascorbic acid per volume of urine.}$$

The result is reported in mg./hr., the normal range considered both at the Massachusetts General Hospital and this hospital to be 29-49 mg./hr. in either postloading 2- or 4-hour specimen. The highest value in our hands was almost invariably in the 4-hour specimen, which, however, in rare instances, was approximately equal to the 2-hour specimen.

Group III consisted of 10 additional cases in which closer attention was paid to clot retraction, clot lysis, quantitative fibrinogens, in addition to the aforescribed base line tests which were carried out as in Groups I and II. Moreover, any abnormal or borderline test was repeated at least once, and—particularly the ascorbic acid saturation test—again repeated at least once after the administration of 300 mg. ascorbic acid or more daily for at least one week.

RESULTS

In addition to classification of the patients into three groups according to what screening tests could be accomplished at the time they were first seen, they were analyzed as to whether or not they had evidence of recent gross or occult hemorrhage. Gross hemorrhage was defined by the presence of hema-

TABLE II
HEMOSTATIC FACTORS IN ACTIVE DUODENAL ULCERS

All 3 groups combined	No. cases with multiple hemostatic defects	No. cases with only 1 hemostatic defect	No. cases with no hemostatic defect
Recent hemorrhage, Gross and occult: 23 cases	14	4	5**
No physical or chemical evidence of recent hemorrhage	1*	0	3

*See text for details of this case.

**Two of these cases (1 with gross, 1 with occult hemorrhage) had platelet counts of well over 500,000, above our normal range. They were the *only* elevated counts among the often repeated ones in the 27 cases. A third had multiple transfusions before the screening tests could be performed.

mesis and/or melena confirmed by guaiac test, with or without shock or acute anemia. Base line studies were done prior to transfusions or ascorbic acid administration, except in rare instances noted elsewhere. Occult hemorrhage was defined by one or more, usually multiple, guaiac positive tests on stools and/or gastric contents in the absence of criteria for gross hemorrhage. None of the occult hemorrhage cases had evidence of chronic anemia and none received transfusions. "Recent" hemorrhage meant usually concurrent with, or within a few days—or occasionally up to 4 weeks—of the time the tests for hemostatic function were completed. In Group I one patient had a subtotal gastrectomy for recurrent massive hemorrhages; another had simple closure of a perforation. In Group II three patients (one the only female) had subtotal gastrectomies for recurrent massive hemorrhage. In Group III one patient had a simple closure for a perforation.

Table I shows that 6 of 8 patients with recent gross hemorrhages had one or more hemostatic defects; 12 of 15 with recent occult hemorrhage had one or more hemostatic defects. There were unfortunately only 4 patients with persistently negative guaiac stools and/or gastric contents. Three of these showed no hemostatic defects. The one case which had hemostatic defects was one of three that had what we have come to consider to be an elevated partial thromboplastin time, namely 137 seconds, and 146 seconds. Even though this was one of the first cases in which this test was used, at which time a number of technical errors were being eliminated by direct observation in our laboratory by the one who introduced us to this test⁹, it was later repeated with better reproducibility, i.e. 112", 112", 111", which however, is still considered at least borderline. In addition, this patient had another "borderline" finding, a bleeding time of 3' 30"

TABLE III
RESULTS OF SCREENING TESTS* FOR HEMOSTATIC DEFECTS IN DUODENAL ULCERS

Test	Platelet count direct with phase microscopy	Bleeding time (Duke-both earlobes)	Clotting time (Lee-White)	Prothrombin time (Quick 1 stage)	Tourniquet test (Rumpel-Leeds)	Partial thromboplastin time	Clot retraction time**
Total no. cases in which performed	24	25	23	27	27	15 (Groups II & III only)	7 (Group III only)
No. cases with abnormal results	8†	5	11	6	4	3	3

*Quantitative fibrinogen levels were done only in the last 6 cases (Group III) and were all well within normal limits (253-604 mg. per 100 ml.)

**See text for frequent serial estimation of per cent of clot retraction as well as gross fibrinolysis of clot simultaneously.

†Abnormally low counts only.

in one ear lobe and 5 minutes in the other. He also had 25-30 petechiae in the tourniquet test, as well as one of the lowest responses to the ascorbic acid saturation test, namely .18, .41, .62, each in mg./hr. in the control, 2-hour and 4-hour postloading specimen. Unfortunately, this patient has been lost to follow-up and repeat tests after conventional medical ulcer treatment, which at that time did not include at least 300 mg. ascorbic acid, which we have since come to consider to be probably close to the usual minimal daily requirement in such cases.

Table II combines the number of cases with recent gross and occult hemorrhage to show the preponderance of these with multiple hemostatic defects. As indicated above in the discussion of the one case with no evidence of recent hemorrhage, but with multiple hemostatic defects, we counted multiple

"borderline" abnormalities as defined more clearly below, in cases under this category, but never listed a case with only one borderline hemostatic defect as one with an abnormal result.

Table III shows the different tests performed for the detection of hemostatic defects, the number of cases with abnormal results (not repeated abnormal results in a given case) as compared with the total number of cases in which the test was done. Platelet counts below 200,000 were considered low (all but one had counts below 180,000). Bleeding times of 3' 30" or over were deemed abnormal, even though 1-3 minutes is often given as the normal range for this method. Even though our laboratory sets 12 minutes as the upper limit for our Lee-White clotting time, "borderlines" of 30 seconds below or above this figure were never counted. Prothrombin times by the 1-stage Quick method usually revealed 12 and 13 second control times, and were never counted if the control exceeded 14 seconds. Percentages below 70 were considered abnormal. There were 6 such cases. Three of the 4 abnormal results of the Rumpel-Leeds tourniquet test were detected in Group III, in which attempts were begun to "refine" this test by comparative serial observations before and after optimal therapeutic repletion of ascorbic acid deficits. More than 10 petechiae in a square inch in the antecubital fossa, however, were required to designate the result of the tourniquet test as positive. The test became negative in these three cases after ascorbic acid repletion but a causal relation has not yet been established.

Three of the 15 cases in which the partial thromboplastin time was carried out showed borderline or abnormal results. The technic and some of the difficulties and merits of this test have been given sufficient attention above for the scope of this paper.

Table IV is self-explanatory and demonstrates again in these cases, what was years ago found by many Americans and British investigators, namely, that ulcer patients generally have low reservoirs of ascorbic acid.

COMMENT

This study was begun about one year ago as an exploratory one and had to be interrupted. It evolved, however, in recent months as a more planned, long-term project, when it continued to be promising even in the face of a growing awareness of the many pitfalls in the technic, accuracy and interpretation of tests of hemostatic function. These pitfalls have been emphasized repeatedly in the book entitled "The Coagulation of Blood"³¹, edited by Tocantins and prepared with the help and under the sponsorship of the Panel on Blood Coagulation of the National Research Council. Some of these difficulties as well as the frequency of false positives and false negatives have been pointed out by Diamond and Porter³².

Jacobson^{33,34} demonstrated the superiority in sensitivity and accuracy of a modification of the "Ivy" bleeding time over the "Duke" method. This as well

as his current arguments in favor of the serum prothrombin consumption test³⁵ as the most sensitive screening test for qualitative platelet defect have influenced us to modify our screening tests accordingly in future new cases and old cases available for follow-up studies. We shall continue, however, to use the clot retraction test in conjunction therewith, since frequent serial observations (1, 2, 4, 6, 12, 24 hrs.) during incubation at 37° revealed impairment of clot retraction in 3 of 7 cases in which it was done. It was borderline, i.e. 80 per cent at 1 hour in one case, and 40 and 50 per cent at 4 hours in 2 others. Surprisingly, gross partial (50 per cent, 50 per cent?) clot lysis appeared in these cases, as well as to a lesser extent in two others, out of 7 in which it was observed for serially.

The real accuracy of these latter observations can not yet be confirmed nor, if actual and beyond the range of normal, be interpreted. These observations will be continued, however, since theoretically increased (partial and early) clot lysis—observable grossly and intermittently—is conceivably due to emotional

TABLE IV
ORAL ASCORBIC ACID SATURATION TEST IN DUODENAL ULCERS

	No. cases test performed in	No. cases with abnormally low results	No. responsive with normal results after 1-5 weeks of 300 mg. ascorbic acid daily
Group II	6	5*	
Group III	10	9*	6**

*One patient had received large doses of ascorbic acid intravenously immediately prior to the test; the other large amounts orally.

**Two of these 6 patients failed to respond adequately to 150 mg. daily. The 3 who failed to respond optimally to 300 mg. daily in 5 weeks or more, required 450 mg. daily in 2 cases, and more in 1 case, to achieve saturation in a few days, but the optimum maintenance dose has not yet been determined for them.

(adrenocortical?) stress or tension, in a manner perhaps similar to that invoked in increased fibrinolysis due to physical activity.

The true explanation for high incidence of 19 cases with one or more hemostatic defects among these 27 cases of active duodenal ulcer is undoubtedly manifold and complex. The importance of technical errors have been discussed to some extent, but those in the performance of the Lee-White clotting time and the "Duke" Bleeding Time would appear to be more likely to create falsely low (negative) rather than falsely high (positive) values. Falsely abnormal results inevitably occur, however, despite honest efforts to the contrary, notably more emphasis on accurate control times in prothrombin times, careful estimate of platelet numbers in blood smears to check direct platelet counts with phase microscopy (helpful *per se* in identification), and the special efforts in training

technicians mentioned above pertaining to the partial thromboplastin time and ascorbic acid saturation test.

The interpretation of results involves, of course, not only evaluation of technical errors, but also the question of normal range, and hence numbers of, and "proved" healthy condition of controls. Even though our controls have, in general, been as expected and especially when correlated with their dietary history in connection with the ascorbic acid saturation test, we plan to increase further the number of our controls as well as a more comprehensive study of them to establish them as "normal" controls, insofar as practical. In this connection, the incidence of latent abnormalities in clotting factors might prove to be surprisingly high (16 per cent) even in a presumably normal population, as published in a preliminary report of 106 medical students by Wright³⁶.

When one considers the numerous exogenous factors in modern civilization (e.g. the ever increasing number of drugs on the market³⁷, dietary excesses especially fats, dietary deficits, especially ascorbic acid, various industrial chemicals, insecticides, air pollutants, etc.), it should not be really too surprising to encounter at least mild abnormalities rather commonly, especially if searched for repeatedly. It is also not difficult to perceive that one or more such potential modifiers of either the hemostatic or fibrinolytic system may become important (i.e. clinical instead of subclinical) in the presence of a site of least resistance, namely a duodenal ulcer, whose size and depth so often does not correlate with hemorrhage. Apart from the question of iatrogenic corticosteroid-induced peptic ulcer, recently considered by Dubois and others³⁸, there is considerable evidence to suggest that excess endogenous secretion of adrenal steroids is a factor in ulcerogenesis³⁹⁻⁴¹. Woldman and his associates have very recently reported⁴² extensive necropsy experience indicative of severity of adrenal damage and focal mucosal hemorrhages and acute ulceration of the upper gastrointestinal tract. They postulate a dual role of the adrenal glands in the pathogenesis of chronic peptic ulcer: an initial acute ulcer during adrenal insufficiency from a stressful situation, followed by hyperactivity of the adrenal cortex resulting in anti-inflammatory action and acid-pepsin hypersecretion, which may disturb the balance between tissue destruction and tissue repair. Whether or not such a dual role might explain apparent discrepancies in the evidence for and against ascorbic acid as obligatory in the biogenesis of adrenal steroids⁴³, it would appear from our evidence and that cited of others that ulcer patients not only often fail to ingest sufficient amounts of this vitamin but require much more than normal controls.

Other investigators have recently revived interest in the theoretical and practical therapeutic and preventive importance of ascorbic acid⁴⁴⁻⁴⁷ in peptic ulcer or "hemorrhagic gastritis". Recent studies on experimental scurvy in guinea-pigs⁴⁸⁻⁵⁰ and observations in a case of human scurvy⁵¹ have revealed that "pure", frank deficiencies of ascorbic acid can produce not only the traditionally

accepted marked vascular defects, but one or more coagulation defects as well. This naturally raises the question as to whether "subclinical" ascorbic acid deficiencies might produce mild coagulation defects which could "summate" with a vascular defect in precipitating or contributing to occult or gross hemorrhage from duodenal ulcer. Our studies on patients in Group III before and after presumed optimal repletion with ascorbic acid exclude some persistent hemostatic defects as due at least solely to ascorbic acid deficiency, but have not been continued long enough to determine how frequent, if ever, such possible etiologic deficiencies might occur in as small a group as this (which, however, will be expanded in the future).

Despite all the above-cited published evidence along these various experimental and clinical lines, as to the potential and actual importance of optimal amounts of ascorbic acid in the treatment and prevention of duodenal ulcer with or without hemorrhage, most diets prescribed for active or healed ulcers have far less of this vitamin than the amount (70-75 mg. daily for adults) in the recommended dietary allowance of the Food and Nutrition Board of the National Research Council. This is recommended in their basic diet for normal adults for prevention of dietary deficiencies.

In her section on "Scurvy" in the 1960 issue of "Current Therapy", Dr. Grace Goldsmith has stated that 10-15 mg. of ascorbic acid daily is believed to prevent (frank) scurvy. She adds, however, that this larger quantity of 75 mg. is recommended because of the many biologic functions of ascorbic acid (especially its role in the intercellular substance and in tyrosine metabolism and its close relationship to adrenal cortical function and stress) as well as the apparent increased requirement in hypermetabolic states and infections of long duration and in acute severe trauma, including burns. Though she makes no specific reference to peptic ulcer, she does state that ascorbic acid may be indicated in amounts greater than those recommended for maintenance of health. One of the deterrents to the use of any or sufficient citrus juices, which contain the highest amounts of Vitamin C, in ulcer diets is the widespread belief that they may irritate the mucosa, but even momentary discomfort can be avoided when such juices are taken at the end, instead of the beginning of a meal, especially breakfast, as is done customarily⁵³.

SUMMARY AND CONCLUSION

Twenty-seven patients with a diagnosis of active duodenal ulcer, confirmed radiographically, were studied with the usual screening tests for hemorrhagic disorders, plus the partial thromboplastin test and oral ascorbic acid saturation test.

Of 23 cases having recent gross or occult hemorrhage, 18 revealed one or more hemostatic defects, despite the absence of "hemorrhagic diathesis" from historical or physical evidence.

Of 16 cases in which the oral ascorbic acid saturation test was performed, 14 revealed low values, most of them grossly low. The two with normal results had received large amounts of ascorbic acid intravenously (immediately) or orally (for months) prior to the test.

Of the 9 patients low in ascorbic acid who could be followed with serial tests 6 responded with normal results after 1-5 weeks of 300 mg. of ascorbic acid daily; the other 3 required 450 mg. or more.

These preliminary results in a small series indicate a surprisingly high incidence of hemostatic defects, despite an increasing awareness of and precautions against the many pitfalls in technics of tests and interpretation of results. The results of the ascorbic acid tests simply confirm results of former investigators that ulcer patients generally ingest far less, yet require much more Vitamin C than the "normal" adult.

Recent experimental and clinical observations, reported especially in the foreign literature, indicate that scorbutogenic defects may consist not only of the traditionally accepted vascular defects, but one or more (intravascular) coagulation defects as well. In addition to these and other possible explanations for some of the hemostatic defects observed by us, emphasis is placed upon the many biologic functions of ascorbic acid and its close relationship to adrenal cortical function and stress and hence to similar important parameters in ulcerogenesis.

It is believed that the following conclusions are warranted:

1. More widespread attention should be paid to optimal ascorbic acid dietary and/or supplementary intakes in both the medical treatment and prevention of recurrences of active duodenal ulcer and its complications.
2. In the evaluation of an ulcer patient for elective surgery, particularly with one or more gross hemorrhages as the complication, the adequacy of previous ascorbic acid intake should be considered, along with the usual other variables, in making the decision.
3. The ideal comprehensive appraisal of an ulcer patient with perhaps even the earliest or intermittent complication should include the most reliable available screening tests for hemostatic function plus a simple oral ascorbic acid saturation test followed by therapeutic titration to "optimal" maintenance dose if necessary, and if reasonably feasible.

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DISCUSSION

Dr. Maxwell Berry (Atlanta, Ga.):—I think that this paper is particularly timely in view of the recent reawakening of interest in Vitamin C and in its multiple somatic functions.

Not so long ago we learned that it was wise to do screening tests for these hemostatic defects in hypertensive patients and more recently in those with atherosclerosis.

From this study I think that we should certainly add the ascorbic acid saturation test and partial thromboplastin times to the usual ones we employ in peptic ulcer.

I was wondering, Dr. Jones, whether these, particularly the ascorbic acid saturation tests, are suitable for the clinicians offices?

Since this is a preliminary study it, of course, leaves some unanswered questions. Does hemorrhage in itself alter the hemostatic mechanisms in ulcer patients?

Does the rate of gastric emptying influence the ascorbic saturation test?

I wish Dr. Jones would comment on possible causes of hemostatic defects other than Vitamin C deficiency. I know we'd be grateful if he would care to comment on these.

I certainly hope that The American College of Gastroenterology will continue to stimulate these preliminary reports. It is exciting to see a man engaged in one line of research find and follow-up an interesting thing in another field. I think this is excellent and we would hope that some day, perhaps through our research committee, we could select preliminary reports that were meritorious and aid them financially and otherwise.

I want to thank Dr. Jones for bringing us this interesting study and hope that next year he is going to present the extension of it.

Dr. H. Leonard Jones (Chelsea, Mass.):—I'm glad Dr. Berry asked several questions that I had tried to answer in the complete manuscript to be published, but which I couldn't, of course, answer verbally for such a complicated subject—in just the few minutes we have here. I think some of them will be answered in the published report better than I can do offhand here, but it does give me a chance to fill in two or three gaps. I think the first question he raised concerned the practicality, for office use, of the ascorbic acid saturation test which we've recently simplified further,—especially since it detects an apparently common and etiologic deficiency factor which is so easily correctable. Whereas formerly it required the patient to submit three urine specimens (control, 2-hour and 4-hour) for chemical analysis, we feel that the 4-hour postloading urine specimen—that is, the specimen collected for the 2- to 4-hour postloading period is sufficient,

because I think virtually in every case this value is the highest value with this test at that particular time. That's the critical value; that's the one we're interested in; if it reaches 29 mg. or more of ascorbic acid per hour, we feel that the patient is saturated and has a reserve sufficient to meet all probable demands of highly variable stresses, hemorrhage, tissue repair, and so forth. . . . Our single specimen procedure, therefore, not only enables us to do three times as many tests, but lends itself admirably to outpatient use. If it cannot be analyzed on collection at the office, it is simply stored in the deep freeze.

There must, of course, be many other causes for these apparently frequent, low-grade or borderline, single or multiple hemostatic defects even though many an ulcer patient appears to have at least "subclinical" deficiency in Vitamin C. This does not necessarily mean of course that he will have even occult hemorrhage, but if he has the right constellation of etiologic factors, for example, high enough gastric acidity along with this and/or other factors, latent hemostatic defect(s) might come to clinical light and be of importance. We are convinced it is certainly worth studying these factors further.

It would not appear to matter too much whether there is an absence of one or more of these mild defects in a series of controls because there is evidence that "controls" will have latent defect(s) that are not important unless there is added a site of least resistance, namely, the peptic ulcer or the other factors in its pathogenesis. In this connection it is interesting that Dr. Irving Wright recently reported in a preliminary study of 106 "normal" medical students that 16 per cent had unsuspected hemostatic deficiencies which caused them no trouble. How many of these were congenital or acquired or whether this percentage held up on studies of more subjects is not known at this time.

When you consider that in our modern civilization there are many possible exogenous causes of subclinical hemostatic defects—various drugs, often too many of them at one time, drug reactions or side-effects from such drugs as reserpine, steroids, salicylates, phenylbutazone, sulfonamides, certain antibiotics, air pollutants, food additives, certain cleaning fluids, etc., there is ample reason, theoretically, and I think we'll find, practically, to explain a number of these, besides ascorbic acid deficits.

A REVIEW OF 300 GASTRECTOMIES*

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In a previous article¹ we presented a report on the status of 175 postgastrectomy patients. Our experience has now been extended to cover 300 cases. In the light of this larger group we have reviewed and re-evaluated our data in an effort to arrive at a truer picture of the postgastrectomy state as seen in our clinic.

As in our former series, the patients were entirely unselected and were interviewed by one of the two physicians in the Gastrointestinal Clinic of Regional Office #3010 of the Veterans Administration in Philadelphia on the basis of a questionnaire as detailed in our previous article. As before, the only two criteria involved were: 1. subtotal gastric resection for duodenal ulcer, and 2. a one-year or longer postoperative period. We again emphasize that we are not concerned with the type of gastrectomy performed, nor the surgical technic involved. Neither are we endeavoring to discover the advantage of one procedure over another. Our sole interest lies in attempting to determine and to evaluate the *over all status* of the postgastrectomy patient. It is what has happened through the years to this so-called "cured" group of patients that prompted our study and continues to sustain our interest.

There were 297 male and 3 female patients in this study.

AGE AND DURATION OF ULCER SYMPTOMS

Age at onset of ulcer symptoms was from childhood to 63 years with 234 patients (78.0 per cent) between 18 and 34 years. The average age at onset was 29.0 years.

Age at time of resection ranged from 18 to 72 years with 242 patients (80.6 per cent) between 24 and 44 years. The average age at operation was 37.8 years.

Age at time of this study was from 19 to 75 years with 240 patients (80.0 per cent) between 28 and 50 years.

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The duration of ulcer symptoms prior to surgery was from one day to 51 years with an average duration of 9.3 years.

TABLE I

Years postoperative	Number of patients	Percentage
1-2 years	73	24.3
2-3 years	48	16.0
3-4 years	35	11.7
4-5 years	36	12.0
5-6 years	20	6.6
6-7 years	27	9.0
7-8 years	8	2.7
8-9 years	13	4.0
9-10 years	14	4.7
10-11 years	12	4.3
11-12 years	4	1.3
12-13 years	4	1.3
13-14 years	2	0.7
15-16 years	2	0.7
19-20 years	1	0.3
26-27 years	1	0.3

It will be seen from Table I that 287 patients (95.7 per cent) in this series were studied from one to 10 years postoperatively.

TABLE II

REASONS FOR SURGERY

Intractability	144 patients	48.0%
Hemorrhage	93 patients	31.0%
Pyloric obstruction	34 patients	11.3%
Perforation	13 patients	4.3%
Previously unsuccessful ulcer surgery	6 patients	2.0%
All others	10 patients	3.4%

Thirty-three patients (11.0 per cent) had undergone surgery for perforated duodenal ulcer from 18 days to 17 years prior to gastric resection. Three of these patients had each had 2 perforations of their ulcer prior to resection.

Three patients with previous posterior gastroenterostomies ranging from 27 years to one year prior to gastrectomy were resected for marginal ulcer. One patient in this category had had a vagotomy and gastrojejunostomy in 1949, a new gastrojejunostomy in 1950 and finally a resection in 1951.

One patient had had a vagotomy with ulcer resection 10 months prior to gastric resection.

TABLE III
WEIGHT STATUS UP TO ONE-YEAR POSTOPERATIVE AS COMPARED TO THE
PREOPERATIVE WEIGHT

Status	Number of patients	Percentage
Loss	269	89.6
Gain	11	3.7
No change	9	3.0
Unknown	11	3.7

One former pyloroplasty was subsequently resected, as was a patient who had been explored 4 years previously, at which time a diagnosis of chronic relapsing pancreatitis had been made.

Two patients each reported 2 former operations on the upper digestive tract, but did not know what had actually been done.

We again advise caution in deciding to operate those patients labelled "intractable" which constituted the major indication in this series (144 patients—48.0 per cent).

TABLE IV
WEIGHT STATUS AT THE TIME OF THIS STUDY FROM 1 TO 26 YEARS.
POSTOPERATIVE

Status	Number of patients	Time postoperative	Percentage
Below preoperative weight	190	1-15 yrs.	63.3
At or over preoperative weight	96	1-26 yrs.	32.0
Unknown	14	?	4.7

In the 269 patients showing weight loss, the loss varied from $\frac{1}{2}$ of a pound to 104 pounds with an average loss of 21.2 pounds.

In the 11 patients showing weight gain, the gain varied from $\frac{1}{2}$ pound to 28 pounds with an average gain of 7.3 pounds.

Only 15 patients (5.0 per cent) were grossly overweight at the time of this study.

NUTRITIONAL STATUS

A total of 84 patients (28.0 per cent) in the entire series ranging from one to 26 years postoperative showed serious impairment of their nutritional status.

The foods in Table VI were the chief offenders, but many other items of food and drink were mentioned from one to 7 times. Multiple food intolerances

TABLE V

Impaired nutrition alone	46 patients	15.4%
Vitamin deficiency alone	13 patients	4.3%
Combined	25 patients	8.3%

often existed in the same patient. Those included in the above list ranged from one to 20 years postoperative.

Fourteen patients (4.7 per cent) from one to 6½ years postoperative had no food intolerance of any kind, yet only 11 of these could eat 3 regular meals a day.

TABLE VI

FOOD INTOLERANCE AND DIETARY HABITS

Sweets	218 patients
Milk	154 patients
Fried foods	113 patients
Greasy foods	102 patients
Spices and spicy foods	100 patients
Crude fiber vegetables	78 patients
Raw fruits	34 patients
Coffee	15 patients
Eggs	15 patients

Seven patients (2.3 per cent) followed a rigid ulcer diet; 11 (3.7 per cent) stipulated a "bland" diet; others complained that breakfast, tobacco, alcohol, rapid swallowing of liquids, fluid at meals, odors, hot food and "almost all foods" affected them.

Ninety-four patients (31.3 per cent) from one to 15 years postoperative were still eating from 5 to 8 small meals a day instead of the traditional three.

One patient, 19 years and 5 months postoperative, was still having all his diet put through a blender.

TABLE VII
GASTROINTESTINAL SYMPTOMS ARISING POSTOPERATIVELY
EXCLUSIVE OF DUMPING

Symptoms	Number of patients	Percentage
Gas	226	75.3
Flatus	225	75.0
Nausea	203	67.7
Belching	190	63.3
Abdominal pain (gastrointestinal)	164	54.7
Vomiting	122	40.6
Variable, poor or no appetite	90	30.0
Diarrhea	44	14.7
Constipation	31	10.3
Alternating constipation-diarrhea	13	4.3

Of the 300 patients only 36 (12.0 per cent) (including the 11 above who had no food intolerance) were able to eat 3 regular meals a day without subsequent discomfort.

TABLE VIII

Type	Number of patients	Percentage
Occasional	58	19.3
Overeating	68	22.7
Mild	39	13.0
Severe	71	23.7

Numerous other gastrointestinal symptoms besides those in Table VII were noted, but not often enough to be significant. The length of time postoperative seems to make little or no difference in the type and intensity of the symptoms.

DUMPING SYNDROME

Two hundred thirty-six patients (78.7 per cent) in this series had some type of dumping syndrome. The over all picture is seen in Table VIII.

Table IX gives the relationship of the dumping syndrome to the number of years postoperative.

Many patients had had dumping in the past which had subsided by the time of this study. These figures represent only those actually having the syndrome at the time of this study.

TABLE IX

Occasional		Overeating		Mild		Severe	
No. of Pts.	Yrs. PO	No. of Pts.	Yrs. PO	No. of Pts.	Yrs. PO	No. of Pts.	Yrs. PO
7	1	14	1	6	1	16	1
18	2	10	2	7	2	11	2
5	3	8	3	2	3	14	3
7	4	8	4	3	4	7	4
4	5	7	5	2	5	7	5
6	6	9	6	5	6	6	6
—	—	3	7	3	7	—	—
5	8	2	8	2	8	3	8
3	9	4	9	1	9	2	9
1	10	—	—	3	10	2	10
—	—	1	11	1	11	2	11
1	12	1	12	1	12	—	—
—	—	—	—	1	13	1	13
1	15	1	15	—	—	—	—
—	—	—	—	1	19	—	—
—	—	—	—	1	26	—	—

Thirty-four (11.3 per cent) had disease involving the liver, gallbladder, pancreas, and rectum, but although these conditions followed gastrectomy we do not attribute them directly to the gastrectomy.

Excluding the 29 cases of glossitis, the 16 cases of marginal ulcer and the 18 cases of upper gastrointestinal hemorrhage loom large.

The tabulation of 16 cases of marginal ulcer is misleading, for if we take into account all the recurrences there were 23 marginal ulcers.

A breakdown of the marginal ulcer cases is given in Table XI.

TABLE X
GASTROINTESTINAL CONDITIONS SUBSEQUENT TO GASTRECTOMY

Conditions	Number of patients	Percentage
Glossitis	29	9.67
Gastritis	8	2.67
Hemorrhagic	1	
Postoperative stomach	4	
Atrophic	1	
Hypertrophic	2	
Gastric ulcer	3	1.00
Marginal ulcer	16	5.33
Upper gastrointestinal hemorrhage	18	6.00
Malfunction of gastrointestinal stoma	4	1.33
Jejunitis	1	0.33
Jejunal ulcer	1	0.33
Jejunal perforation	1	0.33
Intestinal obstruction with or without adhesions	9	3.00

The case in Table XI with the 5 recurrences was operated for "chronic pancreatitis" soon after his gastrectomy. He was later reoperated for marginal ulcer. Since then he has had 5 separate hospitalizations for the medical treatment of his marginal ulcer.

TABLE XI

Number of patients	Number of patients	Years postoperative for recurrences
2	1	—
1	1	2
2	2	—
2	3	—
4	4	—
1	5	—
1	5	6
1	5	7, 7½, 8, 9, 10
2	6	—

Hemorrhage must be considered as a complication of a complication—jejunitis, gastritis, gastric or marginal ulcer.

In short, 90 patients (30.0 per cent) in this series developed gastrointestinal conditions postgastrectomy which we feel are directly attributable to the primary procedure.

TABLE XII

SURGICAL PROCEDURES FOLLOWING GASTRECTOMY AND DIRECTLY RELATED TO IT

Procedure	No. of patients	Time postoperative
1. Dehiscence of abdominal wound	1	10 days
2. Vagotomy	8	1 mo. to 12 yrs.
3. Revision inadequate stoma	3 (4)	1 yr. to 5 yrs.
4. Pancreatitis and marginal ulcer	1	1 yr. & 5 yrs.
5. Adhesions and perforation	2	8 mos. 7 yrs.
6. Adhesions (simple lysis)	1	1 yr.
7. Intestinal obstruction	4 (5)	2 mo. to 7 yrs.
8. Incisional hernia	1	
9. Abscess—gastrectomy wound	1	2 mos.
10. Further resection	1	2 yrs.
11. Subhepatic abscess	2 (3)	3 wks. 1 & 4 mos.
12. Enteroenterostomy	2	4 mos. to 3 yrs.

27 Patients (9%)

SURGICAL PROCEDURES FOLLOWING GASTRECTOMY AND DIRECTLY RELATED TO IT

Vagotomy—8 patients

- 1 mo. postoperative reason unknown.
- 17 mos. postoperative gastritis, presence of free HCl, and pain.
- 18 mos. postoperative marginal ulcer with hemorrhage.
- 2 years postoperative "nervous stomach".
- 2 years postoperative esophageal ulcer with hemorrhage.
- 3 years postoperative marginal ulcer with hemorrhage.
- 3 years postoperative marginal ulcer with hemorrhage and papilloma of the stomach.
- 12 years postoperative marginal ulcer.

Revision of inadequate stoma

1 year postoperative stomal revision plus splenectomy for a "progressively down-hill course".

2 years postoperative intractable vomiting.

3 years postoperative and again at 5 years postoperative for intractable dumping and diarrhea.

Surgery for chronic pancreatitis and marginal ulcer

Pancreatic surgery was performed the same year as gastrectomy. Marginal ulcer surgery was performed 5 years after gastrectomy.

TABLE XIII
NONGASTROINTESTINAL CONDITIONS SUBSEQUENT TO GASTRECTOMY

Condition	Number of patients	Percentage
Fatigue	257	85.7
Cardiovascular disease	24	8.0
Anemia (secondary)	17	5.7
Pain (nongastrointestinal)	15	5.0
Skin diseases	11	3.6
Hypoglycemic attacks	7	2.3
Genitourinary disease	6	2.0
Pulmonary tuberculosis	6	2.0
Vertigo	6	2.0
Weakness	6	2.0

Dehiscence of abdominal wound

10 days postoperative.

Abdominal adhesions and perforation of intestine

8 mos. postoperative obstruction due to adhesions and 10 days later for perforation of the bowel.

7 years 10 mos. postoperative adhesions, obstruction and perforation.

Abdominal adhesions

1 year postoperative simple "lysis of adhesions".

Intestinal obstruction

2 mos. postoperative intestinal obstruction. Eight days later he developed a fistulous tract requiring temporary colostomy. He was unable to work from 17 December 1958 to 3 August 1959 and has 6 abdominal scars from his gastrectomy with vagotomy and the subsequent surgery to combat the complications arising from this "curative" operation.

5 years postoperative.

7 years and 7 mos. postoperative following surgery for jejunal perforation.

2 operations 3 years apart.

TABLE XIV

Weight loss	269 patients	89.7%
Fatigue	257 patients	85.7%
Dumping	236 patients	78.7%
Gas	226 patients	75.3%
Intolerance to sweets	218 patients	72.7%

Incisional hernia—One patient.

Abscess of gastrectomy wound

2 mos. postoperative.

Further gastric resection

2 years postoperative for intractable diarrhea.

TABLE XV

Good	103 patients	34.3%
Fair	133 patients	44.3%
Poor	64 patients	21.4%

Subhepatic abscess

3 weeks postoperative—one patient.

1 and 4 mos. postoperative due to inability to secure adequate closure of the duodenal stump.

Enteroenterostomy

4 mos. postoperative (Same case as immediately above)

Enteroenterostomy, jejunostomy, transection of duodenal stump with secondary closure in a case where the duodenal stump could not be closed at the primary operation. There had been two subhepatic abscesses, abdominal adhesions with partial intermittent bowel obstruction.

Three years postoperative for intractable pain and vomiting. There was a jejunojejunostomy with construction of an Engel Pouch to increase gastric size and to divert the intestinal juices from the mucosa of the gastric remnant.

TABLE XVI

Good	21 patients	19.5%
Fair	52 patients	48.1%
Poor	35 patients	32.4%

These surgical procedures are definitely associated with the gastrectomy preceding them. They involve 27 patients (9.0 per cent) of this series. That is, 27 patients were involved in 15 different surgical procedures subsequent to their original "curative" operation.

It is not our purpose to discuss any possible relationship existing between these postoperative conditions and the gastrectomy which preceded them, but their presence is ominous. Moreover in surveying this series of patients we gain

TABLE XVII

Returned to their original jobs postoperative	151 patients	50.3%
Returned to lighter jobs postoperative	101 patients	33.7%
Never worked postoperative up to the time of this study (1-11 years)	45 patients	15.0%
Attending school under GI Bill	3 patients	1.0%

the distinct impression that they do not enjoy the normal life and health of the average nongastrectomized patient.

From this survey the outstanding symptoms following subtotal gastrectomy are found to be as shown in Table XIV.

RESULTS

The evaluation of our results was on the same basis as explained in our previous paper. Following the criteria there established, we find for this series of 300 cases of subtotal gastrectomy for duodenal ulcer the over all results in Table XV.

Mental status has a very definite bearing on the results obtained, and he who operates patients with some type of mental illness must be prepared to face poorer postoperative results.

In this series there were 39 patients (13.0 per cent) with anxiety neurosis; 23 patients (7.7 per cent) with other types of mental illness; and 46 patients (15.3 per cent) classified as "psychoneurosis", "functional overlay", etc. This gives a total of 108 patients (36.0 per cent) with some type of mental problem, including 3 patients who made a total of 5 attempts at suicide.

The results in these 108 patients differ greatly from the over all results (Table XVI).

Subtotal gastrectomy also has a very definite bearing on the socioeconomic status of the individual, as evidenced by Table XVII.

This problem was considered in some detail in our previous communication, and will form the subject of a subsequent paper.

CONCLUSIONS

As a result of the above findings, and many more in our possession which time and space do not permit us to include, we continue in our previous opinion that subtotal gastrectomy for duodenal ulcer is a highly unsatisfactory procedure, and one which is beset by many serious problems from the initial selection of the patient for surgery throughout the remainder of his life.

Perhaps our contention is one of semantics, but we cannot agree that the patients we have studied in this series are "cured" as is so optimistically stated on their hospital discharge sheets.

REFERENCE

1. Ricketts, Rowland and Straub, E. L.: Gastrectomy and after. *Am. J. Gastroenterol.* **34**:275-292 (Sept.), 1960.

DISCUSSION

Dr. Emil Gribovsky (Huntington, W. Va.):—Here today we've had the report of a study of 300 cases, analyzed in many directions with the conclusion that subtotal gastrectomy for duodenal ulcer is an unsatisfactory procedure in that distressing symptoms and weight loss follow.

When one reads the voluminous literature referring to surgical procedures or intervention for the intentioned cure of duodenal and gastric ulcer one gains the impression that all is not well with the nonmedical treatment of such cases.

Let me at this time indicate to you our efforts in the analysis and treatment of subtotal gastrectomized patients. These are all veterans with service-connected disability by reason of surgical intervention for benign duodenal and gastric ulcer.

(Slide) The type of case that we would like to have operated upon is intractable-duodenal ulcer, perforating or penetrating ulcer or ulcer with recurrent hemorrhage.

(Slide) This is a complete obstruction of the pylorus and duodenum with retention of food, which we believe is the proper case for which surgery should be used.

(Slide) This is a subtotal gastric resection with the initial phase of what is known as hyperperistalsis or as deemed by others a dumping.

(Slide) This is more of the same indicating the rapid emptying of the gastric remnant into the small bowel.

(Slide) These are the operative indications for our series of 100 cases; intractability 34 per cent; hemorrhage, 31 per cent; perforations, 16; obstruction, 16 per cent and gastric ulcers, 3 per cent.

This is somewhat similar to the studies made by Dr. Ricketts and Dr. Straub and you will notice the marked similarity with the exception of obstruction; our obstructive cases are a little higher.

(Slide) The postoperative weight loss in our series was that of 1-10 lbs. (14 per cent); 11 to 20 pounds (28 per cent); 21 to 30 pounds (35 per cent); 31 to 40 pounds (10 per cent) and 41 to 50 pounds (9 per cent), indicating marked weight loss.

(Slide) We institute a regular systematized dietary management in which the patients are given high protein, high fat and low or no carbohydrate diet; and this indicates the weight gain after such therapy.

There is a rather significant weight gain in 47 per cent of the cases. As far as the 46 per cent in which no follow-up was recorded these refer to patients who could not come in for many reasons, because of distance; some coming into the hospital from a distance of about 160 miles.

(Slide) The studies in another section at some distance from this Philadelphia area indicates that there are similarity of results in many postgastrectomized patients. We are markedly interested in the rehabilitation of the individual so that he can once more assume his natural role as a citizen in his home

community, continue as a wage-earner so that his family can survive. I believe this really points up the method that I think is necessary to use in the management of these cases.

The results were: Excellent, there were 54 per cent, those who returned to work, full-time, and those who had very few, little or no symptoms. Fair results: were those who returned to part time work—and this represents 6 per cent of the cases; Poor results: were those who did not return to work at all or who were living in unemployed areas and could not obtain work or who applied for work and were turned down by the employer.

Dr. Ricketts' and Dr. Straub's paper indicates the disabilities that occur after gastrectomy and it certainly gives thought for the future handling of these cases. Our series, I think, corroborates their studies very closely. There is very little argument as far as the results. We might argue about definitions of dumping syndrome or the types of cases that are suitable for subtotal gastrectomy.

Otherwise I think that our cases actually confirm their results and I'm sorry that we have not much argument here.



Coca-Cola, too, has its place in a well balanced diet. As a pure, wholesome drink, it provides a bit of quick energy ... brings you back refreshed after work or play. It contributes to good health by providing a pleasurable moment's pause from the pace of a busy day.





President's Message

This month we carry the program of the Central Regional Meeting, the fourth of this year's sessions, elsewhere in the issue.

The third meeting will be that of the New York Chapter to be held in New York City on Monday, 10 April 1961.

This is indeed an excellent start for Regional Meetings, and I sincerely hope that they will continue to be held in the years to come. I am sure those who attend will agree that they have a definite purpose and serve to bridge the gap between Annual Meetings.

Speaking of Annual Meetings, it is still not too late to send in your application for the presentation of a paper. We would like to include on the program as many of our own College membership as possible.

By this time the applications for Scientific Exhibit space have also been sent out. Those of you who have seen the exhibits at our last few conventions, were much impressed by the excellence of the presentations and the quality.

Since available space is generally limited, may I suggest that you mail in the application form as soon as possible, so that it may be considered by the committee.

Henry Baker

NEWS NOTES

CENTRAL REGIONAL MEETING

The Central Regional Meeting of the American College of Gastroenterology will be held in Milwaukee, Wisc., on Sunday afternoon, 16 April 1961. The sessions will be held at the Schroeder Hotel, commencing at 2:00 P.M., following the Semi-Annual Meeting of the Board of Trustees of the College.

The program is under the Chairmanship of Dr. Edwin A. Ellison, with Drs. Robert T. McCarty, M.C.F. Lindert, Michael W. Shutkin and Philip O'Neil, members of the committee.

The General Chairman of the meeting is Dr. Robert T. McCarty, Governor of the College for Wisconsin.

The Central Region consists of the states of Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota and Wisconsin.

Program

1. Newer Trends in Chemotherapy of Advanced Gastrointestinal Cancer—
Dr. John Hurley, Milwaukee, Wisc.
2. Considerations in Surgical Treatment for Duodenal Ulcer—
Dr. Deward O. Ferris, Rochester, Minn.
3. Leucine Aminopeptidase Studies in Pancreatic and Biliary Diseases—
Dr. LeRoy Sims, Madison, Wisc.
4. Endoscopic Diagnosis of Certain Lesions of the Bowel (Motion picture)—
Dr. Raymond J. Jackman, Rochester, Minn.
5. Management of Ulcerative Colitis with Special Reference to Steroids—
Dr. Jean Spencer, Chicago, Ill.
6. Gastrointestinal Manifestations of Cerebral Diseases—
Dr. Andrew E. Cyrus, Jr., Milwaukee, Wisc.

In Memoriam

We record with profound sorrow the passing of Dr. E. James Buckley, New York City, N. Y., Fellow and Dr. John B. Karr, Chicago, Ill., Member of the American College of Gastroenterology. We extend our deepest sympathies to the bereaved families.

ABSTRACTS FOR GASTROENTEROLOGISTS

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STOMACH

PERFORATION OF THE STOMACH IN THE NEWBORN: E. Malcolm Field. *J. Michigan M. Soc.* 58:1262 (Aug.), 1959.

Perforation of the stomach in the newborn is uncommon. Sixty cases have been reported, to which the author adds four more with three survivals. In order of descending frequency the causes are perforating gastric ulcer, hypoplasia or agenesis of portions of the gastric musculature, trauma, including nasogastric tubes and sepsis. The clinical picture is that of an infant, often premature, who following birth seems to be doing satisfactorily. Then there is a dramatic episode. The child's respirations become labored with periods of intermittent cyanosis, regurgitation of blood tinged formula and bloody stools. The abdomen quite suddenly becomes distended. Bowel sounds may be present but soon disappear as peritonitis with adynamic ileus develops. The diaphragm is elevated and often there is no percussion liver dullness. Frequently there is edema of the skin with erythema which may be mistaken for cellulitis associated with omphalitis. Occasionally subcutaneous emphysema with distinct crepi-

tus develops in the abdominal wall. Cultures are negative for clostridia. It is thought that air passes from the abdomen along the umbilical cord to the abdominal wall. Roentgen evidence of massive pneumoperitoneum is almost always present. If gastric intubation is carried out, x-ray may show that the tube protrudes from the stomach. If the perforation occurs into the lesser peritoneal cavity through the posterior gastric wall, air may not be seen under the diaphragm; but a mass may be found in the upper mid abdomen from the gastric contents in the lesser sac extending down between the layers of the omental apron which as yet are not fused. As soon as diagnosis is made, fluid and electrolytes are administered and operation performed under local anesthesia. Antibiotics are not used unless there has been a positive peritoneal culture. The only hope for survival is prompt diagnosis and surgical intervention.

SAMUEL L. IMMERMAN

MANAGEMENT OF PROFUSE GASTROINTESTINAL HEMORRHAGE: A. M. Snell. *Am. Pract. & Digest. Treat.* 10:1315 (Aug.), 1959.

The author believes that all hospitals should have a hemorrhage team set up to deal with cases of gastrointestinal bleeding.

He bases his proposal on the fact that the mortality rate in profuse gastrointestinal hemorrhage continues to be very high. He

makes the point that an increasing number of causes for acute gastrointestinal bleeding is now being recognized and that a more vigorous diagnostic approach is indicated. Such approach is to include the

physical examination, laboratory aids, including bromsulfalein, endoscopy and roentgen studies. The treatment can thus be quickly and properly instituted.

IRVIN DEUTSCH

GASTRIC PSEUDODIVERTICULUM: Peter J. Kapo. Pennsylvania M. J. 62:1339 (Sept.), 1959.

A case of gastric pseudodiverticulum secondary to pancreatic pseudocyst was reported and x-ray evidence presented to corroborate this.

Laparotomy revealed that one of the loculations of the inflammatory pancreatic pseudocyst was located within the lesser

omental sac and impinged upward into the gastric fundus causing a forceful invagination of the cyst into this region. The temporary fundal sac disappeared after aspiration of the pseudocyst and marsupialization was performed.

MORTON SCHWARTZ

DUODENAL FISTULAS FOLLOWING SUBTOTAL GASTRECTOMY: Joseph J. Schechter and David W. Barrow. Illinois M. J. 116:140 (Sept.), 1959.

The authors are reporting on a series of subtotal gastric resections with postoperative duodenal fistula formation in five patients, which was an incidence in their series of 2 per cent of their gastrectomies.

All of the resections were of the Hofmeister type with antecolic anastomosis.

The signs and symptoms of duodenal stump blowout are those of peritonitis from any cause plus external leakage of duodenal contents when this is possible.

The diagnosis must be suspected in any patient following a gastric resection who develops more or less sudden upper abdominal pain with right upper quadrant tenderness and laparotomy carried out as soon as possible. The authors' five patients devel-

oped this complication from the third postoperative day to the 32nd postoperative day.

Treatment consists of laparotomy, removal of escaping secretions by constant suction, maintenance of the nutrition and meticulous care of the skin. The best treatment is, of course, prevention.

All of the various methods of handling the duodenal stump are discussed. The mortality rate in this series of five amounted to 40 per cent. This complication is more likely to occur in patients with large areas of edema and inflammation around the ulcer and patients who develop obstruction of the duodenal loop.

PAUL LEDBETTER

PEPTIC ULCER: CHOICE OF PROCEDURE IN OPERATIVE TREATMENT: Russell J. Crider and Ben L. Neubeiser. Missouri Med. 56:1026 (Sept.), 1959.

This article is not a statistical study, but rather a critique on the choice of operative procedure for the cure or palliation of peptic ulcer. It would be wise for the interested reader to read the article directly since it would be almost impossible to abstract the facts without quoting the whole paper. The basic thesis pleads for an evalu-

ation of the patient with the choice of an appropriate procedure dependent on age, habitus, complications, location of the ulcer, temperament and occupation. Operative procedures should not be done merely to prove a certain procedure is a success by running a series of unselected cases.

STANLEY STARK

GASTRIC ATONIA AND DELAYED GASTRIC EMPTYING AFTER VAGOTOMY FOR OBSTRUCTING ULCER: W. F. Bergin and Paul H. Jordan, Jr. Am. J. Surg. 98:612 (Oct.), 1959.

The problem of delayed gastric emptying in patients operated upon for obstruct-

ing duodenal ulcers has been studied. Seventy-two consecutive patients operated

upon for obstructing duodenal ulcer were studied. In 8 of 32 patients with obstruction, treated by vagotomy and complementary drainage procedures, gastric retention developed which persisted longer than ten days. One patient died as a result of this complication.

Delayed gastric emptying did not occur in any of the 42 patients with pyloric obstruction, treated by subtotal gastric resection. There were no deaths in this group.

In a series of 44 patients treated by vagotomy and ancillary drainage proce-

dures for reasons other than pyloric obstruction, there was no instance of delayed gastric emptying and there was no mortality.

The authors are of the opinion that subtotal gastric resection is the treatment of choice for patients with obstructing duodenal ulcer. The results of this study suggest that vagotomy and a complementary drainage procedure is not a conservative operation, in patients with pyloric obstruction.

CARL J. DEPRIZIO

INTESTINES

BONE METASTASES FROM CARCINOMA OF COLON AND RECTUM. E. Delannoy and M. Martinot. *La Presse Medicale* 67:2049-2052 (Nov.), 1959.

Four observations are presented. Two of them concern metastases of the spine and scapulohumeral area, occurring 4 years respectively after resection of sigmoid cancer and amputation of rectal carcinoma. In the two other cases, metastases were found simultaneously with right colic cancer and sigmoid carcinoma, respectively on one rib, skull and clavicle.

Statistically, frequency of such metastases is 1 to 3 per cent; much less than from breast, prostate, thyroid and even gastric cancer.

The different methods of cancer cells embolization are reviewed: 1. by the way of portal vein, two filters have to be crossed

over (liver and lung) before reaching systemic circulation. 2. by the portacaval shunt represented by hemorrhoidal veins, only the lung acts as a filter between the primary tumor and arterial circulation. 3. finally the venous system of the spinal cord offers another way for metastatic cells.

Symptomatology is not different from other bone metastases but the lytic form is more frequent at roentgen examination.

When looking back to primary cancer, in the presence of apparently isolated bone metastases, one has to research rectal or colic carcinoma, after one has eliminated the more usual primary localizations.

GUY ALBOT

DUODENAL MOBILIZATION IN GASTRECTOMY: Mandel Weinstein, Morton Robert and Brian Reynolds. *Am. J. Surg.* 98:713 (Nov.), 1959.

The purpose of this study is to describe a planned type of operative procedure found to be valuable during the past four years in almost all operations for duodenal ulcer, in which the lesion was considered resectable. The most difficult part of gastrectomy for duodenal ulcer is the mobilization of the duodenum. This is described whereby the operation proceeds along planes of normal tissue, thus avoiding trauma to the surrounding important structures. The dissection for mobilization begins at the inferior safe zone to the right of the inferior border of the duodenum just beyond the pylorus. The upper extremity of

the pancreaticoduodenal adhesion is approached through the superior safe zone by sectioning the superficial layer of the hepatoduodenal ligament.

A list of complications in mobilization is described and includes injuries to the pancreatic duct, trauma to the bile duct and duodenum resulting in fistula, as well as pancreatitis. These observations were studied over a period of four years.

Of a total of 170 gastrectomies performed for patients with duodenal ulcer, according to this technic, all but one patient recovered from surgery and left the hospital with well healed wounds. There

was one fatal case of a patient with acute pancreatitis, and one patient with a non-fatal duodenal fistula.

The authors do not advise planned mobilization of the duodenum for any ulcer

that lies in a vulnerable part of the duodenum, but instead advocate surgical treatment in a much safer manner.

CARL J. DePRIZIO

RUPTURE OF AN ABDOMINAL AORTIC HOMOGRAFT, WITH ILEAL FISTULA:
Lester A. Hagland, William R. Sweetman and Robert A. Wise. *Am. J. Surg.* 98:746 (Nov.), 1959.

Although the initial results of arterial homograft replacement have been brilliant, it is apparent that ruptures are becoming more common. Such an occurrence is reported in an aortic bifurcation arterial homograft three years after resection of an abdominal aortic aneurysm.

Since most ruptures have occurred in the early postoperative period, it is difficult to account for one after three years. The site of rupture in their patient could have been at an aneurysmal dilatation of a branch stump.

A case report of a 62-year old white male, who developed three aortic ileal fistulas resulting in severe hemorrhages into the intestines within a short period of time is given. There was a successful repair of the first two ruptures, but the last one was fatal.

The authors believe that in view of the rapid recurrence of the aortoileal fistula, after the initial suture, that local repair of the defect is hazardous. Complete replacement is certainly the procedure of choice.

CARL J. DePRIZIO

HYPOPROTEINEMIA ANTEDATING INTESTINAL LESIONS, AND POSSIBLY DUE TO EXCESSIVE SERUM LOSS INTO THE INTESTINE: H. Holman, W. Nickel and M. Slesinger. *Am. J. M.* 27:963 (Dec.), 1959.

Six patients are reported with "idiopathic" hypoproteinemia and rapid loss of albumin and gamma globulin from the plasma. The appearance of hypoproteinemia antedated the development of intestinal lesions in three of these patients.

Albumin and gamma globulin have been demonstrated in the intestinal juice of these patients and of normal persons. The possibility exists that the hypoproteinemia is a

consequence of excessive loss of serum protein into the intestine.

Experiences with treatment are presented. Two patients improved greatly after resection of diseased intestine.

Although all the intestinal lesions appeared to be inflammatory, no specific pathological classification was possible.

JOHN M. McMAHON

LIVER AND BILIARY TRACT

THE PATHOLOGY OF PSITTACOSIS, A REPORT OF TWO CASES WITH HEPATITIS: E. M. Yow, J. C. Brennan, J. Preston and S. Levy. *Am. J. Med.* 27:739 (Nov.), 1959.

The clinical features of turkey-borne psittacosis are described as they were observed in an outbreak infecting 24 of 40 workers.

Two of the patients infected in this epidemic exhibited clinical and laboratory evidence of hepatitis with renal decom-

pensation. One of the patients died and autopsy findings revealed a severe interstitial pneumonitis with tracheobronchitis, acute toxic nephrosis, acute nonspecific reactive hepatitis, and multiple focal lymphocytic meningitis.

JOHN M. McMAHON

SURGICAL ASPECTS OF BILIARY TRACT DISEASE: C. H. Richardson, Jr. J.M.A. Georgia 48:563 (Nov.), 1959.

As a result of a review of 150 surgical procedures of the biliary tract the author recommends removal of all diseased gall-bladders with or without calculi unless the operative risk is prohibitive.

A concerted effort to discover and correct common duct pathology is indicated.

The use of operative cholangiography is indicated whenever common duct pathology is suspected but not in the large solitary calculus with small ducts and no jaundice. Its use in the elderly is questioned because of increased operating time.

GLENN S. ROST

PORTAL VENOUS PRESSURE IN "PIPESTEM", FIBROSIS OF THE LIVER DUE TO SCHISTOSOMIASIS: A. H. Aufses, F. Schaffner, W. S. Rosenthal and B. E. Herman. Am. J. Med. 27:807 (Nov.), 1959.

PORTAL HYPERTENSION DUE TO SCHISTOSOMIASIS MANSONI. M. R. Garcia-Palmieri and P. A. Marcial-Rojas. Am. J. Med. 27:811 (Nov.), 1959.

Two cases of schistosomiasis are described. In the first, a case of portal hypertension with esophageal varices due to schistosomiasis is presented in which the wedged hepatic vein pressure was normal whereas the splenic pulp pressure and mesenteric vein pressure were high. The hepatic involvement was of the type described as "pipestem" fibrosis, an instance of extraparenchymal portal fibrosis. The resulting portal hypertension is similar in genesis to that of extrahepatic portal vein obstruction rather than to the intrasinusoidal hypertension characteristic of true cirrhosis.

The second case—a patient with portal hypertension due to *schistosomiasis man-*

soni who withstood 33 episodes of hematemesis is described.

In this case there was marked portal hypertension accompanied by minor alterations in liver function tests and in the structure of the liver parenchyma. These differences are important in the clinical differentiation of this disease from patients with portal hypertension due to portal cirrhosis of the liver.

Decompressive portal surgery is tolerated better in patients with portal hypertension due to schistosomiasis than in those with portal cirrhosis, because of the lesser degree of parenchymatous hepatic damage.

JOHN M. McMAHON

JAUNDICE DUE TO PROCHLORPERAZINE: F. A. Solomon, Jr. and F. A. Campagna. Am. J. Med. 27:840 (Nov.), 1959.

A case of jaundice due to prochlorperazine (compazine) is presented, with pertinent laboratory data including liver biopsy. The jaundice was of the intrahepatic ob-

structive type resembling in every way that reported in association with the administration of chlorpromazine.

JOHN M. McMAHON

IDIOPATHIC HEMOCHROMATOSIS: T. Bothwell, I. Cohen, O. Abrahams and S. M. Perold. Am. J. Med. 27:730 (Nov.), 1959.

Fifty-two immediate relatives of six patients suffering from idiopathic hemochromatosis were examined. In 11 subjects with raised serum iron levels three were found to have the fully developed disease while five others showed varying degrees of iron excess on liver biopsy.

These results support the concept that idiopathic hemochromatosis is a familial

disorder in which the absorption of excessive amounts of iron from the gut eventually leads to massive accumulation of iron within the body. The disease is probably the result of a autosomal genetic defect of incomplete penetrance and/or variable expressivity which is transmitted as a Mendelian dominant.

JOHN M. McMAHON

LIVER CELL NECROSIS IN CHLORPROMAZINE JAUNDICE (ALLERGIC CHOLANGIOLITIS), A SERIAL STUDY OF TWENTY-SIX NEEDLE BIOPSY SPECIMENS IN NINE PATIENTS: Am. J. Med. 27:708 (Nov.), 1959.

Nine patients with chlorpromazine jaundice were studied for periods varying from 43 days to over three years. Twenty-six needle biopsy specimens of the liver were obtained in these nine patients, varying from one to five biopsy specimens per patient.

Although much less prominent than in viral hepatitis, necrosis of liver cells is found in chlorpromazine jaundice, notably in the centrilobular zones adjacent to the evidences of cholestasis, and frequently also in periportal intralobular extensions of the portal exudate. It is accompanied and followed by intralobular liver cell regeneration, characterized both by multinucleation and by mitosis. The necrosis of liver cells is reflected in rises in serum glutamic-pyruvic transaminase, and to lesser degree in serum glutamic-oxaloacetic transaminase. The findings suggest that necrosis of

liver cells (hepatitis) may play a more important role in the causation of chlorpromazine jaundice than is generally recognized.

The disease histopathologically is of prolonged duration compared with the transitory symptomatology. This duration is reflected in the laboratory measurements, particularly in the serum alkaline phosphatase, and often in persisting eosinophilia. There was no evidence in these cases of the development of permanent residual damage or fibrosis in the liver, although a transient portal fibrosis was observed to follow resolution of the portal infiltrations.

Disorganization and necrosis of interlobular bile ducts, followed by their regeneration, occurred in the two most severe cases of this series.

JOHN M. McMAHON

PATHOLOGY AND LABORATORY RESEARCH

EFFECT OF GONADECTOMY ON EXPERIMENTAL PEPTIC ULCERATION: G. B. Singh and R. C. Shukla. Indian J. M. Res. 47:287 (May), 1959.

Experimental studies were undertaken to study the effect of gonadectomy on gastric mucosa and gastric secretion of normal rats and on the degree of ulceration in pyloric-ligated rats.

It was noted that ovariectomized rats showed increased degree of gastric ulceration and significantly higher values of peptic activity than nonovariectomized rats.

The possible mechanism of enhanced ulceration was discussed.

It was found that orchidectomy did not influence either the gastric secretion or the degree of ulceration.

Also observed was the fact that gonadectomy alone, without ligation, had no ulcerogenic effect on the gastric mucosa.

MORTON SCHWARTZ

NEOMYCIN IN THE CONTROL OF OUTBREAKS OF INFANTILE GASTROENTERITIS: W. Roberts and B. A. Woodger. Scottish M. J. 4:228 (May), 1959.

An attempt was made to evaluate the effectiveness of neomycin as a prophylactic agent in the control of infantile gastroenteritis in a gastroenteritis ward of the authors' hospital in Glasgow, Scotland. Since neomycin has no systemic toxic effects when given orally and has other advantages over such antibiotics as streptomycin, chloramphenicol, tetracycline, etc., it was felt to be most suitable for prolonged administration. The method used was to treat all patients admitted to the gastroenteritis ward with neomycin until

dismissed. This procedure was adopted for three months and the cross-infection rate was then compared with that obtained for the previous three months and observations were made on the effect of neomycin on the fecal excretion of serological types of *E. coli*.

In the first period of general treatment there were 86 admissions of which 27 (31.4 per cent) were excreting *E. coli* on admission. There were 28 cross-infection incidents involving 26 (35.7 per cent) patients. In the study period 97 patients were

admitted. Twenty (20.6 per cent) were positive on admission. There were only four (4.1 per cent) cross-infection incidents during this period. Twenty-eight out of 31 positive cases (92 per cent) treated with neomycin for 5 days or continuously

to dismissal became negative within an average of 2.1 days. The control of an outbreak of infantile gastroenteritis in a children's pneumonia ward is described.

LOUIS A. ROSENBLUM

LACTIC DEHYDROGENASE ACTIVITY IN GASTRIC JUICE IN THE DIAGNOSIS OF GASTRIC CANCER: A PRELIMINARY REPORT: Steven Schenker. Am. J. Digest. Dis. 4:412-418 (June), 1959.

A remarkable discovery may be hidden in this publication notable for its brevity and modesty. The interested reader will remember that dehydrogenase is an enzyme capable of mobilizing hydrogen from a substrate and enabling it to be acted upon by a hydrogen acceptor, a coenzyme. Lactic dehydrogenase oxidizes alpha hydroxy acids to alpha keto acids. The author based his experiment on Wroblewski's observation of lactic dehydrogenase (LD) activity in serous effusions caused by des-

quamated carcinoma. In applying this observation the author determined LD activity in the nonacid gastric juice of four groups of patients. Group 1, consisted of 11 normal controls; group 2, of eight with uncomplicated pernicious anemia; group 3, of seven with benign gastric ulcer; group 4, of seven with gastric cancer. LD activity was markedly higher in group 4 than in groups 1, 2, and 3.

WALTER CANE

GLUCURONIDE FORMATION IN PATIENTS WITH CONSTITUTIONAL HEPATIC DYSFUNCTION (GILBERT'S DISEASE): Rudi Schmid and Lydia Hammaker. New England J. Med. 260:1310 (25 June), 1959.

Six patients with Gilbert's disease and 9 normal controls were studied after administration of N-acetyl-p-aminophenol non-toxic compound that is excreted in the urine as a glucuronide. No difference in plasma concentration or in urinary excretion of the glucuronide was observed between icteric and control subjects. These findings fail to support the concept that in Gilbert's disease a defect in the glucuronide transference systems in the liver is responsible for the retention of nonconjugated bilirubin in the plasma. It is con-

ceivable but unlikely, however, that different enzyme systems are responsible for the formation of aminophenyl glucuronides and of bilirubin glucuronide. Also NAPA conjugation may occur outside the liver and thus would fail to reflect a possible defect in bilirubin glucuronide formation. The authors believe however it more likely that the defect involved is one of transport of nonconjugated bilirubin to the liver cell rather than a defect of glucuronide formation.

RALPH D. EICHORN

HEPATIC INVOLVEMENT IN EXTRAPULMONARY TUBERCULOSIS. R. J. Korn, W. F. Kellow, P. Heller, Bernhard Chomet and H. J. Zimmerman. Am. J. Med. 27:60 (July), 1959.

Hepatic function was studied in 50 patients with extrapulmonary tuberculosis. Abnormalities of one or more of the liver function and/or serum protein tests were found in all patients. The most frequent changes were impaired bromsulfalein excretion and hyperglobulinemia.

Liver biopsy specimens were obtained in 30 of these patients. Granulomas were demonstrated in 24 or 80 per cent of the specimens. Fourteen of the 15 patients

with elevated alkaline phosphatase levels had hepatic granulomas as did ten of the 15 patients without alkaline phosphatase elevation. Microgranulomas were described and were considered significant. Focal Kupffer cell hyperplasia and diffuse sinusoidal inflammatory reaction were sufficiently frequent to be characteristic of hepatic involvement in tuberculosis.

JOHN M. McMAHON

BIOCHEMICAL, BLOOD GAS AND PERIPHERAL CIRCULATORY ALTERATIONS IN HEPATIC COMA. M. P. Tyer and H. O. Sieker. *Am. J. Med.* 27:50 (July), 1959.

Biochemical and blood gas measurements were obtained in 49 patients with a variety of liver diseases.

A progressive increase in arterial ammonia concentration with increasing cerebral dysfunction was observed.

The presence and extent of coma correlated more closely with arterial than peripheral venous ammonia concentrations.

The patients with cerebral dysfunction exhibited a significantly greater respiratory

alkalosis than alert patients. It appeared likely that the alkalosis contributed to the disordered consciousness.

Marked variation of arterial oxygen saturation was observed.

None of the findings noted were necessarily of prognostic significance. However the presence of azotemia with associated oliguria was seen only in patients who died.

JOHN M. McMAHON

RECTAL CORTISOL IN THE THERAPY OF ULCERATIVE COLITIS: A.M.A. Arch. Int. Med. 104:260 (Aug.), 1959.

To evaluate the efficacy of rectal cortisone a solution of 200 mg. of Solu-Cortef in 100 c.c. of saline was instilled rectally once daily to a number of patients. Others received saline enemas and served as controls. Clinical response to cortisone therapy was satisfactory in a number of persons with mild and moderate changes and a history of recent onset. Severe and extensive involvement of the colon and prolonged

duration of the disease were contraindications to this form of therapy as it was ineffective. A few of the successfully treated patients showed relapse 48 hours after cessation of therapy. This was demonstrated by repeated rectoscopic examinations. Rectal cortisone is particularly useful in some patients where systemic use of steroids is contraindicated.

H. B. EISENSTADT

EFFECT OF ANTIPERISTALTIC GUT SEGMENTS ON INTESTINAL EMPTYING TIME: J. M. Hammer. *J. Michigan M. Soc.* 58:1289 (Aug.), 1959.

The authors studied the effect of the insertion of a reversed intestinal segment. It has long been held that such a reversal is fatal to animals. In animals in which 75 and 80 per cent of the small intestine was removed and no segment reversed, all animals died within three months of cachexia. In the same experiment in which Pamine was added to the diet, four of the six animals survived but proved difficult to maintain because of the side-effects from large doses of the drug. In animals in which 80 to 90 per cent of the small intestine was removed and the distal inch of the remaining small bowel was reversed and reinserted in an antiperistaltic manner,

9 of the 12 animals survived for two years and maintained weight. The short reversed segment acts to delay emptying time, causes marked hypertrophy and dilatation of the intestine, permits digestion to proceed, with a normal blood chemistry. In humans with mesenteric thrombosis, trauma, regional ileitis and fistula, but especially in mesenteric thrombosis, it may be necessary to remove 80-90 per cent of the small bowel. Conceivably a reversed segment in such patients might prevent starvation, cachexia and a fatal outcome of many such patients.

SAMUEL L. IMMERMAN

DETECTION OF ACHLORHYDRIA BY TUBELESS GASTRIC ANALYSIS WITH BETAZOLE HYDROCHLORIDE AS THE GASTRIC STIMULANT: Harry L. Segal, James C. Rumbold, Bernard L. Friedman and Michael M. Finigan. *New England J. Med.* 261:544 (10 Sept.), 1959.

A study was undertaken to compare the efficacy of Betazole Hydrochloride as compared with caffeine as the gastric stimulant

in the detection of achlorhydria by the tubeless gastric analysis technic. Of 149 patients found to be achlorhydric with the

use of caffeine as the gastric stimulant 51 per cent were found to have free hydrochloric acid after the use of 50 mg. of Histalog orally. In a group of patients using 100 mg. of Histalog there was no significant increase in the percentage of acid secretors as when the 50 mg. dose was used.

In a group of 86 persons tested by simultaneous intubation and a tubeless procedure with a 50 mg. dose of Histalog by mouth as the stimulant there was revealed 8 false negative (9 per cent) and two false positive (2 per cent) reactions as compared with a previous statistic with the use of caffeine as the gastric stimulant, in which there was 7 per cent false nega-

tive and 3 per cent false positive reactions. The authors speculate that the slightly higher percentage of false negative tests with the use of Betazole Hydrochloride may be due to some indirect action of the compound on the absorption or excretion of the Azure A dye, as used in the tubeless technic.

The side-effects with the use of the 50 mg. dose of this compound were insignificant, and therefore, the authors conclude that Betazole Hydrochloride is a safe and effective stimulant in the detection of achlorhydria by the tubeless gastric analysis.

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1. *British Medical Journal* 2:827, 1955

2. *American Journal of Gastroenterology* 28:439, 1957

BOOK REVIEWS FOR GASTROENTEROLOGISTS

A TEXTBOOK OF MEDICINE: Edited by Russell L. Cecil, M.D., Sc.D., Professor of Clinical Medicine Emeritus, Cornell University, Robert F. Loeb, M.D., Sc.D., D. Hon. Causa, LL.D., Bard Professor of Medicine, Columbia University, Associate Editors: Alexander B. Gutman, M.D., Ph.D., Professor of Medicine, Columbia University; Walsh McDermott, M.D., Livingston Farrand, Professor of Public Health and Preventive Medicine, Cornell University; Harold G. Wolff, M.D., Professor of Medicine (Neurology), Cornell University. Tenth Edition, 1665 pages, illustrated, W. B. Saunders Co., Philadelphia, Pa., 1959. 1 Vol. Price \$16.50. In 2 Vols. Price \$20.50.

When a volume of this type reaches the tenth edition, there is no doubt that it is an authoritative text which incorporates the latest developments in pathological physiology and also covers subjects which have not been included in previous editions. Despite the inclusion of this new material there has been no limitation of clinical discussion.

In addition to the previous contributors the editors have added new ones to replace those who died between editions.

Medical students, physicians and even

faculty members of undergraduate and graduate medical schools, physicians preparing for the written and/or oral Board examinations are advised to read systematically this fountain of information.

Normal laboratory values of clinical importance plus the index enhance the value of the text.

The editors, the contributors and W. B. Saunders, the publishers, are to be commended for bringing out this beautifully printed, illustrated and bound volume.

HYPERTENSION—The First Hahnemann Symposium on Hypertensive Disease: Edited by John H. Moyer, M.D., Professor and Chairman of the Department of Medicine, Hahnemann Medical College and Hospital, with the assistance of John R. Beem, M.D.; Robert Bower, M.D.; Joseph DiPalma, M.D.; Arthur Grollman, M.D.; William Likoff, M.D.; Lewis C. Mills, M.D., 790 pages, illustrated, W. B. Saunders Co., Philadelphia, Pa., 1959. Price \$14.00.

It would take many pages to describe this monumental volume on hypertension. In order not to delay the review, the reviewer feels that only after re-reading carefully the entire text will he be able to report on the outstanding contributions and the numerous suggestions for diagnosis and

treatment.

It is, however, highly recommended to all physicians as a most useful working text on hypertension and Dr. Moyer, his co-workers and the publisher are to be congratulated on their untiring efforts.

DIGESTIVE SYSTEM, UPPER DIGESTIVE TRACT, Part I of Volume III: Prepared by Frank H. Netter, M.D. Edited by Ernst Oppenheimer, M.D., The Ciba Collection of Medical Illustrations, 206 pages, 172 full-color illustrations with descriptive text, Commissioned and published by Ciba, 1959. Price \$12.50.

Nine consultants and contributors have made possible the publication of this most excellent and authoritative volume of the upper digestive tract. Medical students, doctors preparing for licensing examinations or specialty boards, will be greatly benefited by reading the text and studying the illustrations. General practitioners, specialists in gastroenterology, dentists and oral surgeons will find diseases of the mouth and pharynx a veritable mine of information. Not only does it deal with normal and abnormal

states, it also depicts the various manifestations found locally and in systemic diseases. It is unbelievable that the authors and the artist, Dr. Netter, have been able to show all these lesions in one volume.

The diseases of the esophagus, pages 148 to 156, are excellent. From here on the reviewer was entranced with the section on the stomach by Dr. Nissen.

Extensive references and cross index complete the text.

This is a most remarkable presentation

and the price is intended only to meet the cost. It is recommended to all those who need a handy reference. It serves its purpose well, as a reference book for teachers,

undergraduate and graduate medical and dental students, general practitioners and specialists.

MANUEL DE GASTROSCOPIE PRATIQUE: Edited by Alexandre d'Oblonsky with a preface by Dr. Raymond Dupuy, 55 pages, paper cover, Masson & Cie, Paris, France, 1959. Price 950 Fr.

Although only 54 pages, the text is sufficient to orient the gastroscopist on the necessary precaution in the use of the gastro-

scope, the preparation of the patient, the introduction of the instrument, and the findings in a given case.

DAS DIAGNOSTISCHE PNEUMOPERITONEUM: Prof. Dr. Med. A. Gebauer, Frankfurt, A/M, with an introduction by Professor Dr. F. Hoff, Director the 1st Medical University Clinic, Frankfurt, A/M, 69 pages, illustrated, Georg Thieme Verlag, Stuttgart, Germany, 1959. Price \$4.30.

Pneumoperitoneal diagnosis, which at one time was performed more often, now has been revived in some institutions. Where abdominal diagnosis by x-ray is not feasible or questionable or where liver puncture does not yield the desired information, Pneumoperitoneal diagnosis may often aid the surgeon in arriving at a more accurate means of determining the state of the ab-

dominal organs and the peritoneum.

The newer methods have again stimulated this procedure and have been found a useful guide in determining the presence or absence of adhesions or even tumors, before laparotomy.

Although the text is written in German, the illustrations are clear and depict the idea conveyed by the author.

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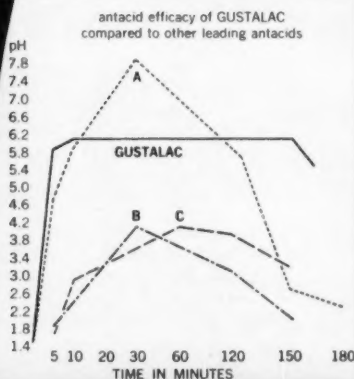
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1. Kirstner, J. B.: J.A.M.A. 166:1727, 1958.



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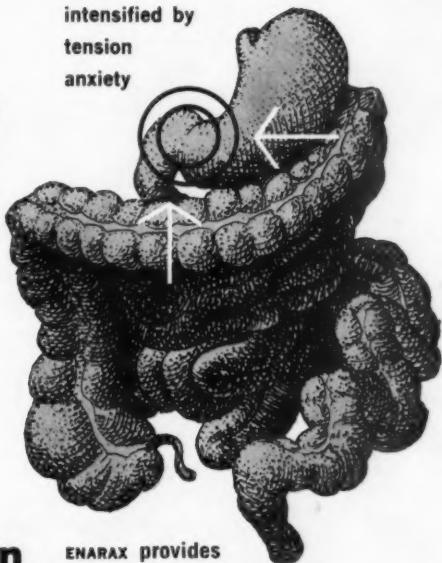
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References: 1. Hock, C. W.: *Am. J. Gastroenterol.* 34:293 (Sept.) 1960. 2. Leming, B. H., Jr.: *Clin. Med.* 6:423 (Mar.) 1959. 3. Data in Roerig Medical Department files.

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1. Nesselrod, J. P.: *Clinical Proctology*, ed. 2, Philadelphia, Saunders, 1957. 2. Page, S. G., Jr., et al.: *J. A. M. A.* 157:1208, Apr. 2, 1955. 3. Gross, J. M.: *J. Internat. Coll. Surgeons* 23:34, Jan., 1955. 4. Page, S. G., Jr., et al.: *Gastroenterology* 32:747, Apr., 1957. 5. Hellman, L. D.: To be published.

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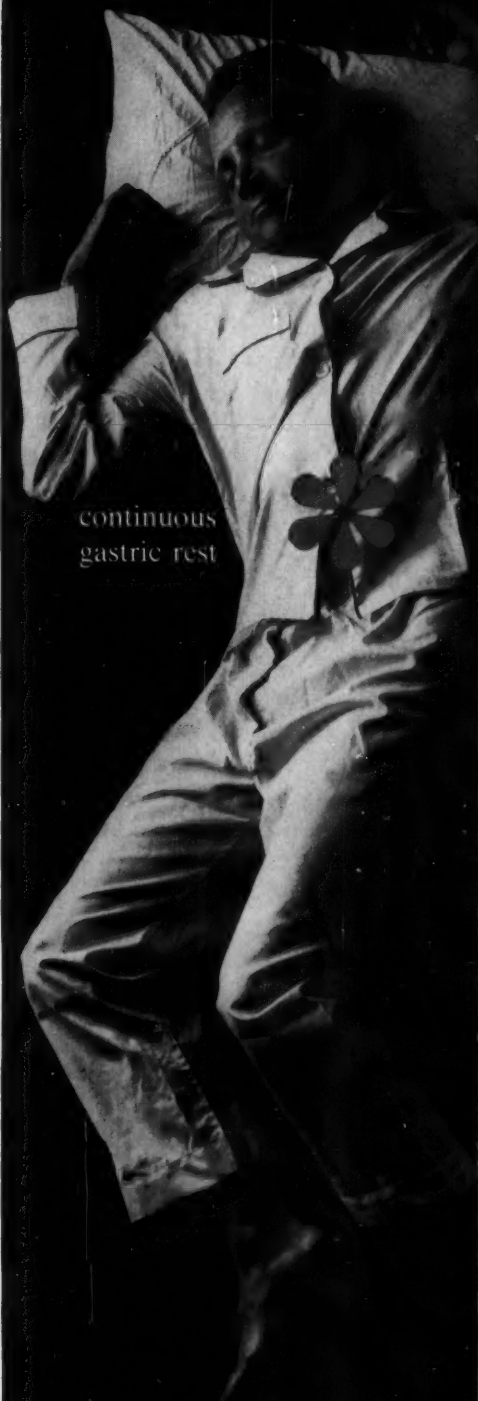
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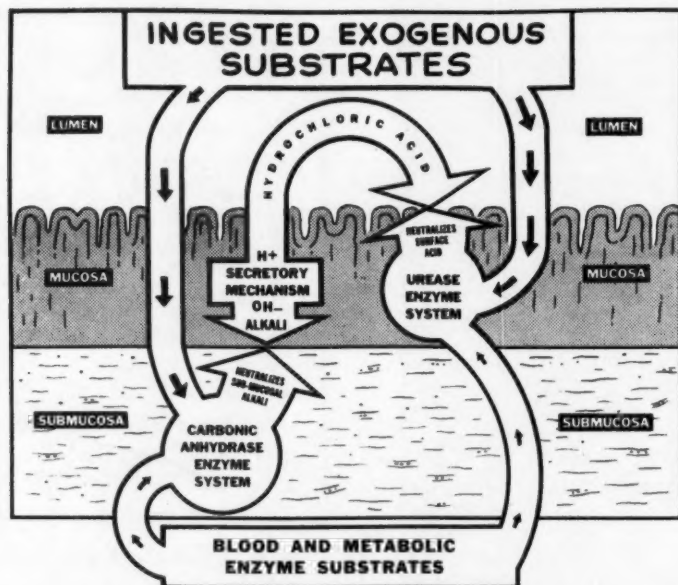
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- (1) Goodfriend, Vanderkleed & Goodfriend. "Enzymatic Therapy of Peptic Ulcer and Digestive Disorders." American Journal Gastroenterology, Vol. 33, No. 1, Pgs. 80-89, January 1960.
- (2) Kelly, H. T., M. D., "Treatment of Gastrointestinal Ulcer and Certain Digestive Disorders with Mucosal Enzyme Substances", American Journal of Gastro., Vol. 33, No. 12, December, 1960.



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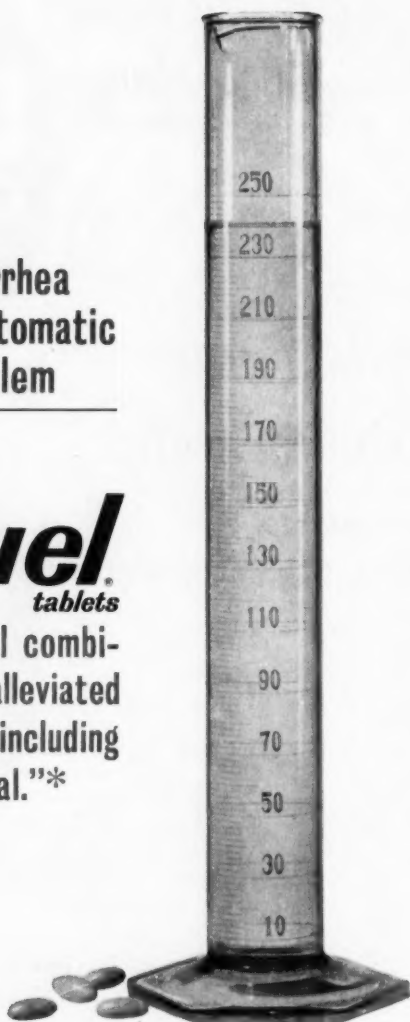
1. Weiss, J.: Amer. J. Gastroent., July 1960.
2. Breidenbach, L. and Secor, S. M.: Amer. J. Surg., Jan. 1957.

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^{*}Winkelman, A.: *Am. J. Digestive Dis.* 34:524 (Nov.) 1960; additional bibliography: Hock, C.W.: *Med. Times* 88:320 (March) 1960; Hock, C.W.: *Am. J. Digestive Dis.* (Nov.) 1960; Berkowitz, D.: *Am. J. Digestive Dis.* (Nov.) 1960; Suarez, H.: *Am. J. Digestive Dis.* (Nov.) 1960; Gilbert, A. S.; Schwartz, I. R., and Matzner, M. J.: *Am. J. Gastroenterol.* (Dec.) 1960; Gilbert, S. S.: *Am. J. Digestive Dis.* (Nov.) 1960; Pimparker, B. D.; Paustian, F. F.; Roth, J. L. A., and Bockus, H. L.: *Gastroenterology*, to be published; Roth, J. L. A.: *Am. J. Digestive Dis.* (Nov.) 1960; Grossman, A. J.; Batterman, R. C., and Leifer, P.: *J. Am. Geriatr. Soc.* 5:187 (Feb.) 1957; McHardy, G.; Browne, D.; McHardy, R.; Bodet, C., and Ward, S.: *Am. J. Gastroenterol.* 24:601 (Dec.) 1955; McHardy, G.: *Am. J. Digestive Dis.* (Nov.) 1960; Berkowitz, Z. T.: *J. Am. Geriatr. Soc.* 5:940 (Nov.) 1957. Reports to the Medical Department, White Laboratories, Inc.

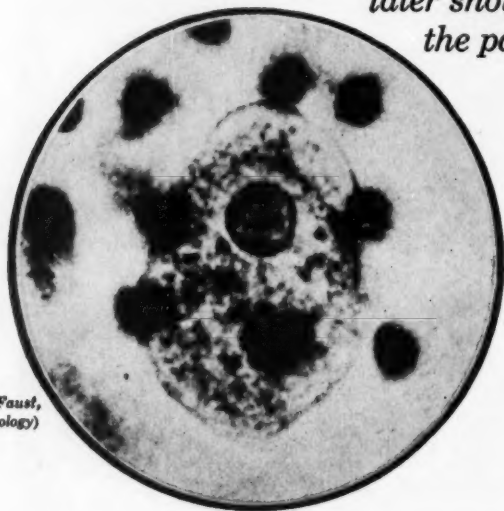
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1. Frye, W.W., and Lampert, R.: Treatment of Asymptomatic *Endameba histolytica* Carriers with a Formulation of Bacitracin-Methylene Disalicylate and Iodochlorhydroxyquin (Anameba). *Am. J. Gastroenterol.* 34:429-432 (Oct.), 1960.

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constipation

SURFAK®

Water doesn't roll off this duck's back . . . because the water is Surfak-treated. Surfak decreases interfacial tension between water and oil . . . penetrates the natural oils in the feathers, permits water absorption, adding weight so that the duck sinks.

Similarly, in functional constipation, Surfak quickly permeates the heterogeneous fecal mass. The superior surfactant action of calcium bis-(dioctyl sulfosuccinate) reduces the interfacial tension between the aqueous and lipoid phases of the intestinal content to minimal values. The result is soft homogeneous feces which are easily moved to evacuation, naturally.

DOSAGE:

Adults: One 240 mg. Surfak capsule daily.
Children (and adults with minimal needs): One to three 50 mg. Surfak capsules daily.

SUPPLIED:

240 mg. Surfak capsules in bottles of 15 and 100. 50 mg. Surfak capsules in bottles of 30 and 100.

LLOYD BROTHERS, INC.

CINCINNATI 3, OHIO

